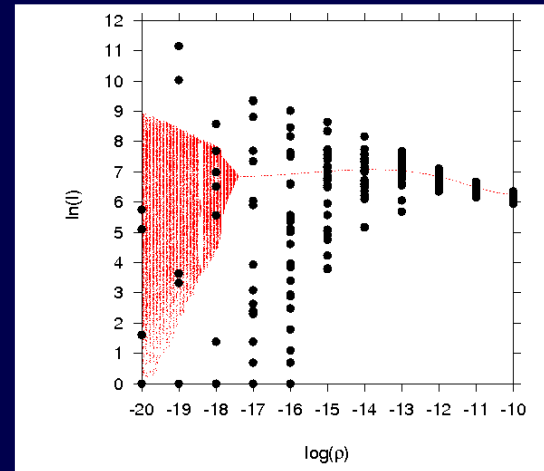
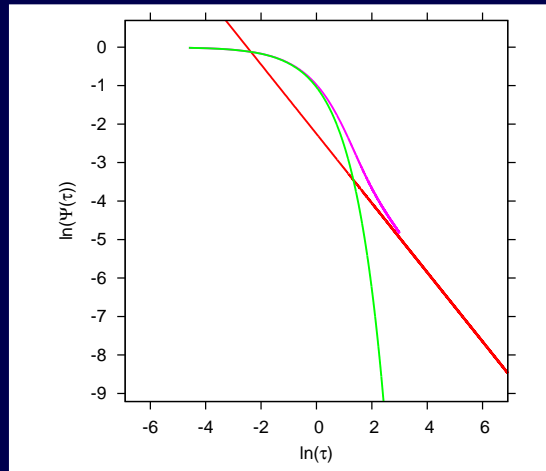


# Power law jumps and power law waiting times, fractional calculus and human mobility in epidemiological systems



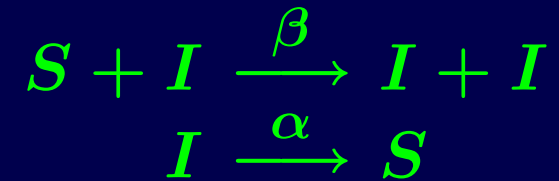
Nico Stollenwerk

Mathematical Biology and Statistics Group

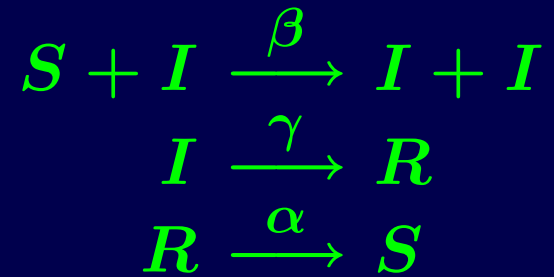
Centro de Matemática, Aplicações Fundamentais  
e Investigação Operacional (CMAF-CIO)  
Univ. Lisboa

# Simplest epidemiological processes

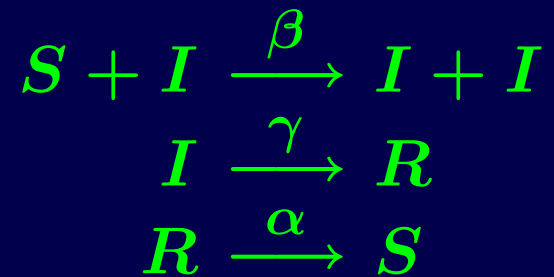
epidemic process: SIS



epidemic process: SIR



## Susceptible-Infected-Recovered epidem.: SIR



gives ODE system

$$\frac{d}{dt} S = \alpha R - \frac{\beta}{N} SI$$

$$\frac{d}{dt} I = \frac{\beta}{N} SI - \gamma I$$

$$\frac{d}{dt} R = \gamma I - \alpha R$$

## SIR system with seasonality

$$\frac{d}{dt} S = \alpha R - \frac{\beta(t)}{N} SI$$

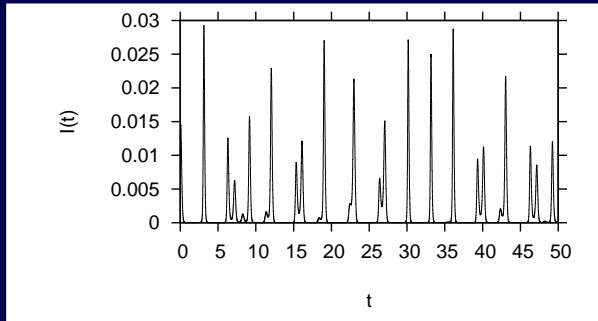
$$\frac{d}{dt} I = \frac{\beta(t)}{N} SI - \gamma I$$

$$\frac{d}{dt} R = \gamma I - \alpha R$$

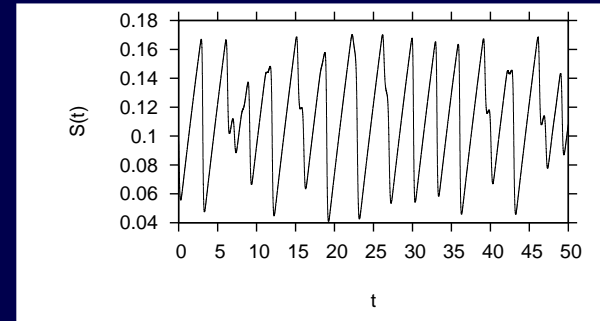
with seasonal forcing of the infection rate

$$\beta(t) = \beta_0 \cdot (1 + \eta \cdot \cos(\omega \cdot t) )$$

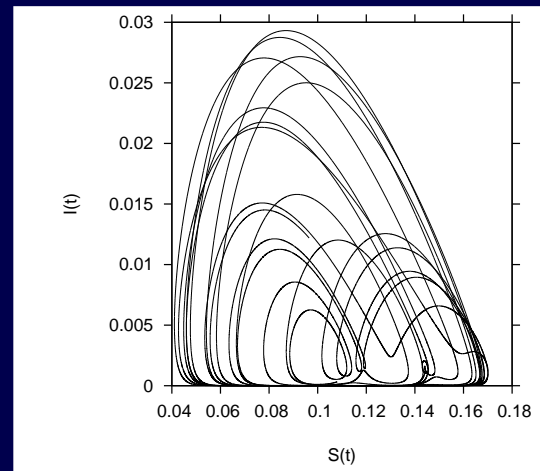
# SIR system with seasonality



time series of  $I(t)$

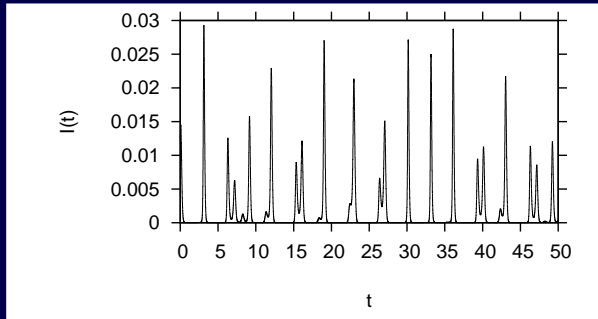


time series of  $S(t)$

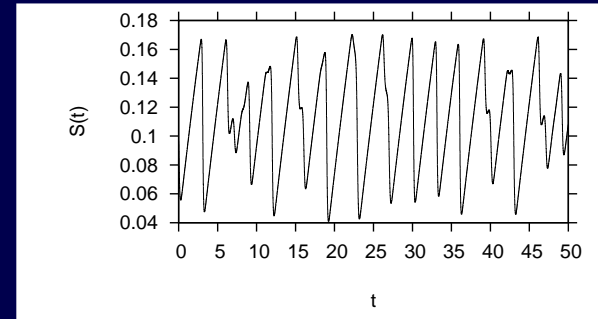


state space plot from time series  
 $I(t)$  versus  $S(t)$

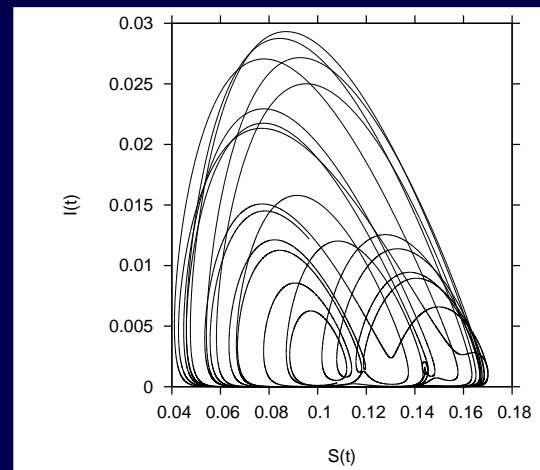
# SIR system with seasonality



time series of  $I(t)$

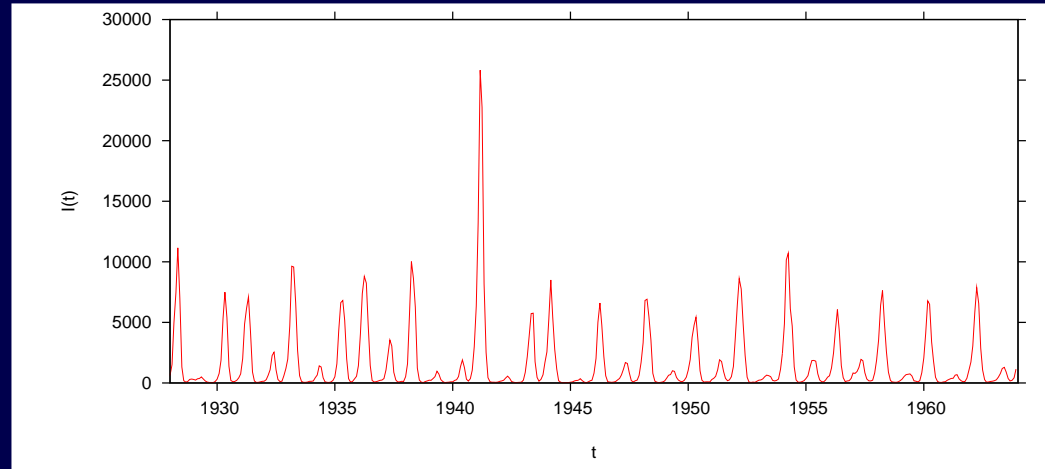


time series of  $S(t)$

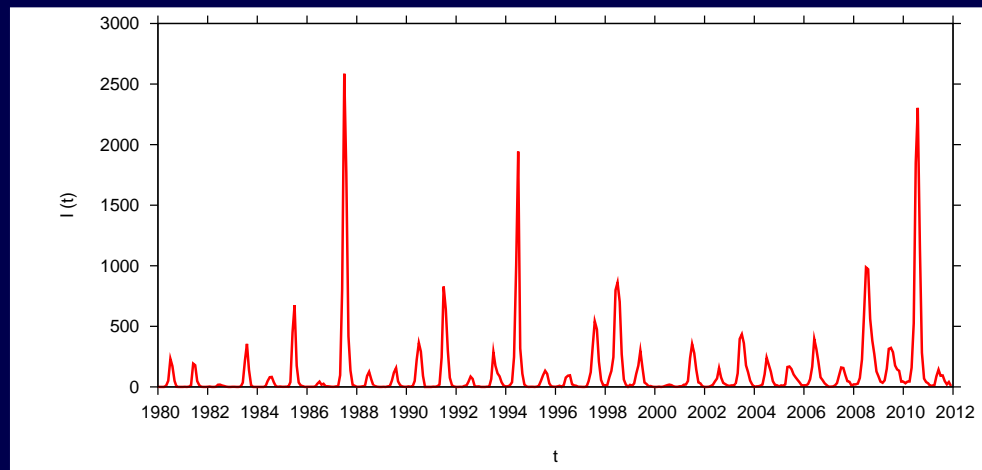


deterministic chaos

# Epidemiological systems with various qualitative features



measles in New York City



dengue fever cases in Chiang Mai (Thailand)

**Explicit multi-strain models:  
example: dengue fever**



**Explicit multi-strain models:  
example: dengue fever**

**simplest example: two-strain SIR model**

**including antibody dependent enhancement (ADE)**

**=> chaos only for large ADE parameter  $\phi$**

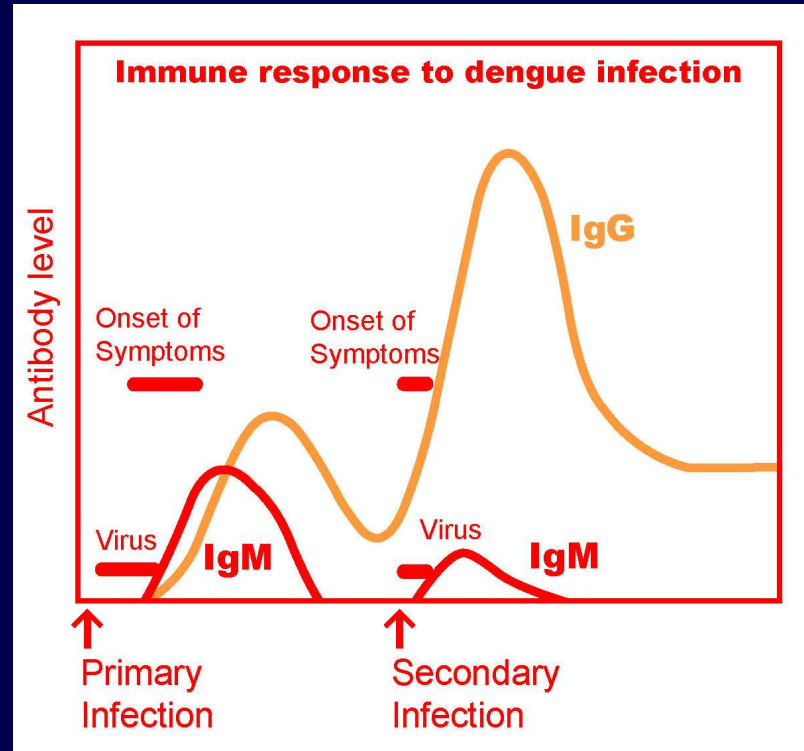
**biologically motivated extension**

**including temporary cross immunity**

**=> chaos for much wider  $\phi$ -region**

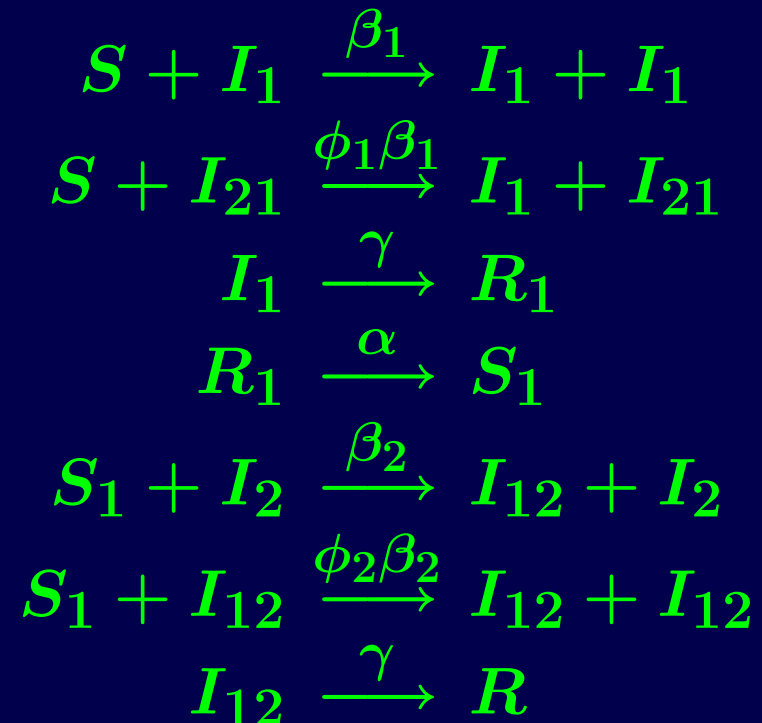
**(also for “inverse ADE”)**

# Antibody dependent enhancement, ADE

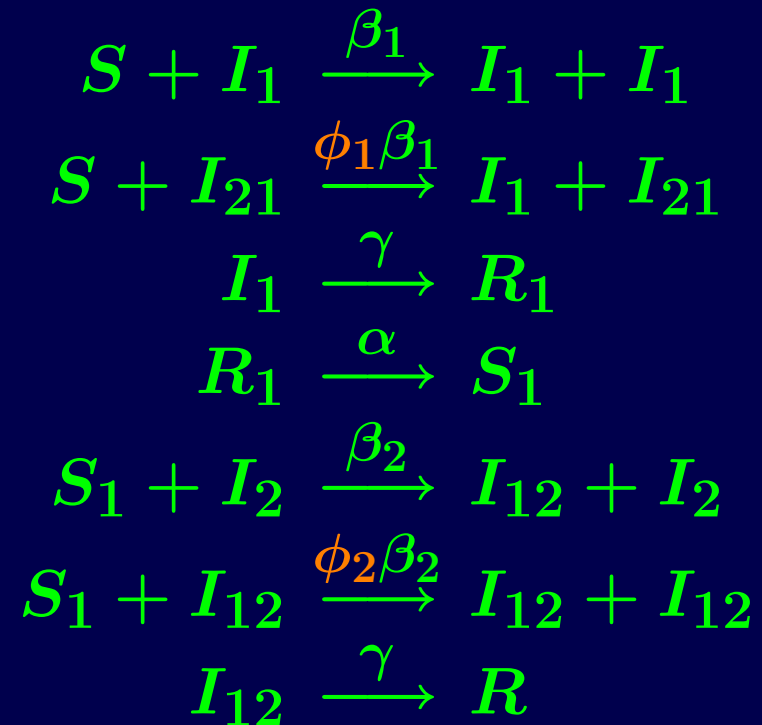


... and temporary cross-immunity

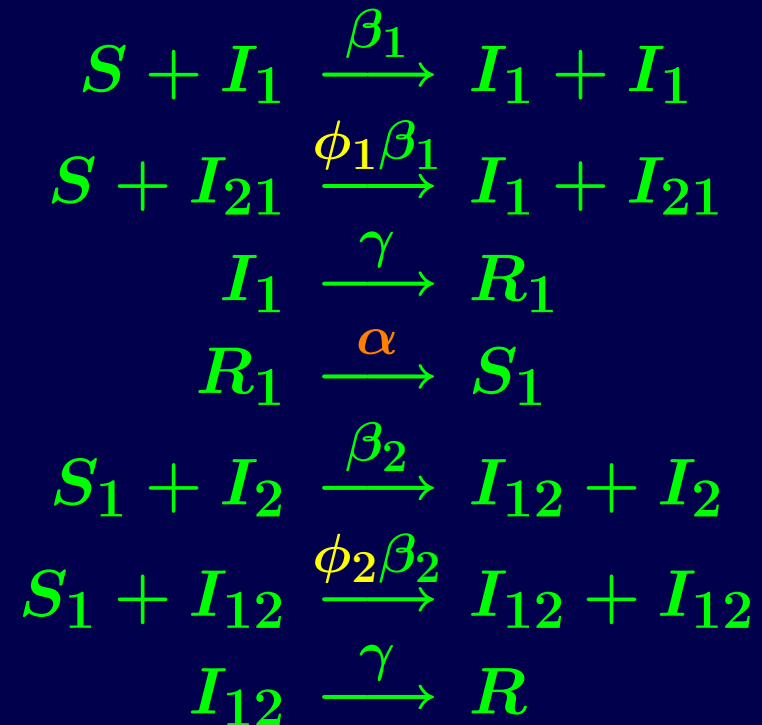
## Transition rates for two-strain SIR model with ADE and temporary cross immunity



## Transition rates for two-strain SIR model with ADE and temporary cross immunity



## Transition rates for two-strain SIR model with ADE and temporary cross immunity



# Multi-strain model for dengue fever

$$\frac{dS}{dt} = -\frac{\beta_1}{N}S(I_1 + \phi_1 I_{21}) - \frac{\beta_2}{N}S(I_2 + \phi_2 I_{12}) + \mu(N - S)$$

$$\frac{dI_1}{dt} = \frac{\beta_1}{N}S(I_1 + \phi_1 I_{21}) - (\gamma + \mu)I_1$$

$$\frac{dI_2}{dt} = \frac{\beta_2}{N}S(I_2 + \phi_2 I_{12}) - (\gamma + \mu)I_2$$

$$\frac{dR_1}{dt} = \gamma I_1 - (\alpha + \mu)R_1$$

$$\frac{dR_2}{dt} = \gamma I_2 - (\alpha + \mu)R_2$$

$$\frac{dS_1}{dt} = -\frac{\beta_2}{N}S_1(I_2 + \phi_2 I_{12}) + \alpha R_1 - \mu S_1$$

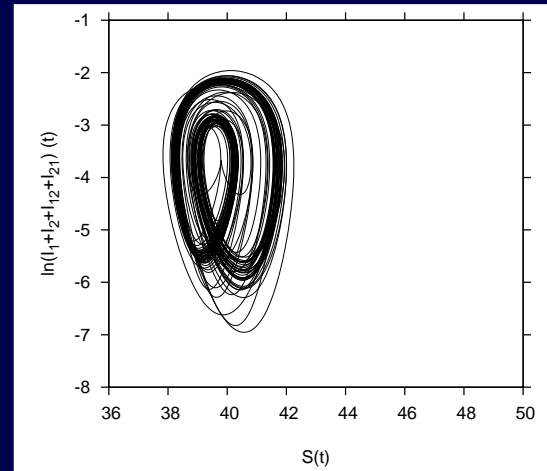
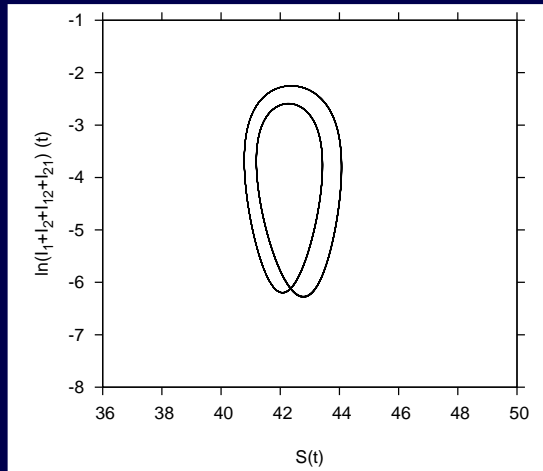
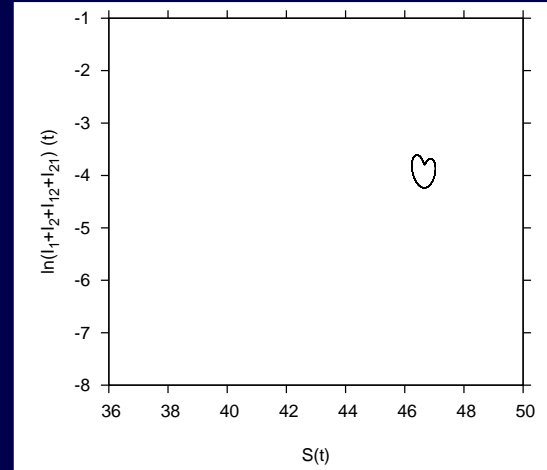
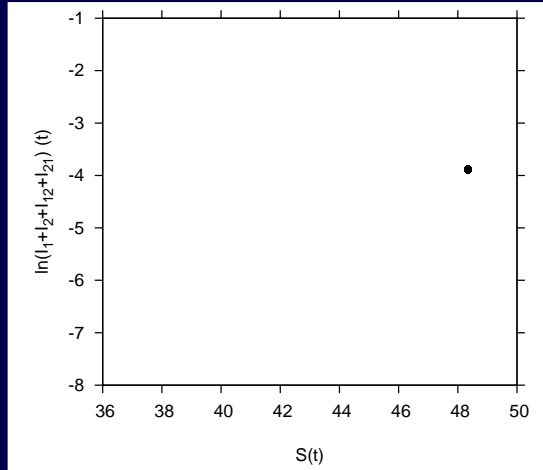
$$\frac{dS_2}{dt} = -\frac{\beta_1}{N}S_2(I_1 + \phi_1 I_{21}) + \alpha R_2 - \mu S_2$$

$$\frac{dI_{12}}{dt} = \frac{\beta_2}{N}S_1(I_2 + \phi_2 I_{12}) - (\gamma + \mu)I_{12}$$

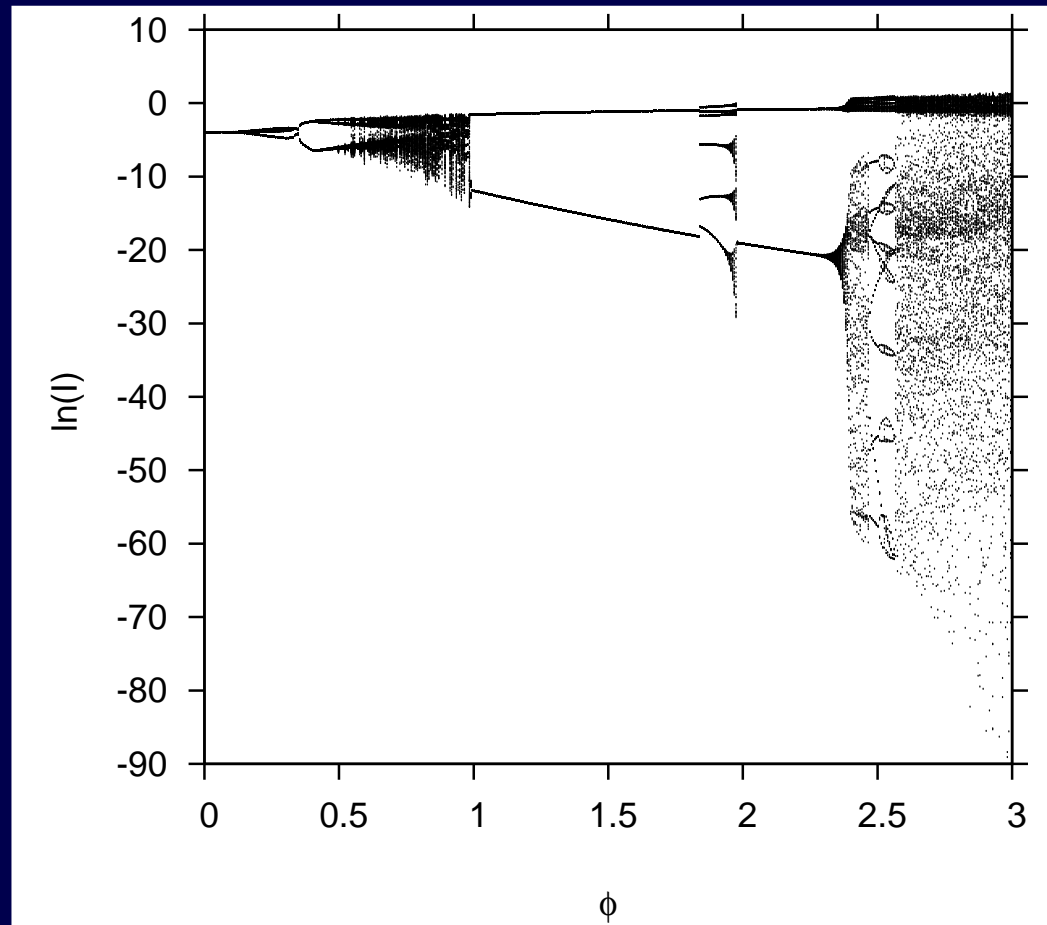
$$\frac{dI_{21}}{dt} = \frac{\beta_1}{N}S_2(I_1 + \phi_1 I_{21}) - (\gamma + \mu)I_{21}$$

$$\frac{dR}{dt} = \gamma(I_{12} + I_{21}) - \mu R$$

# Bifurcations for changing $\phi$



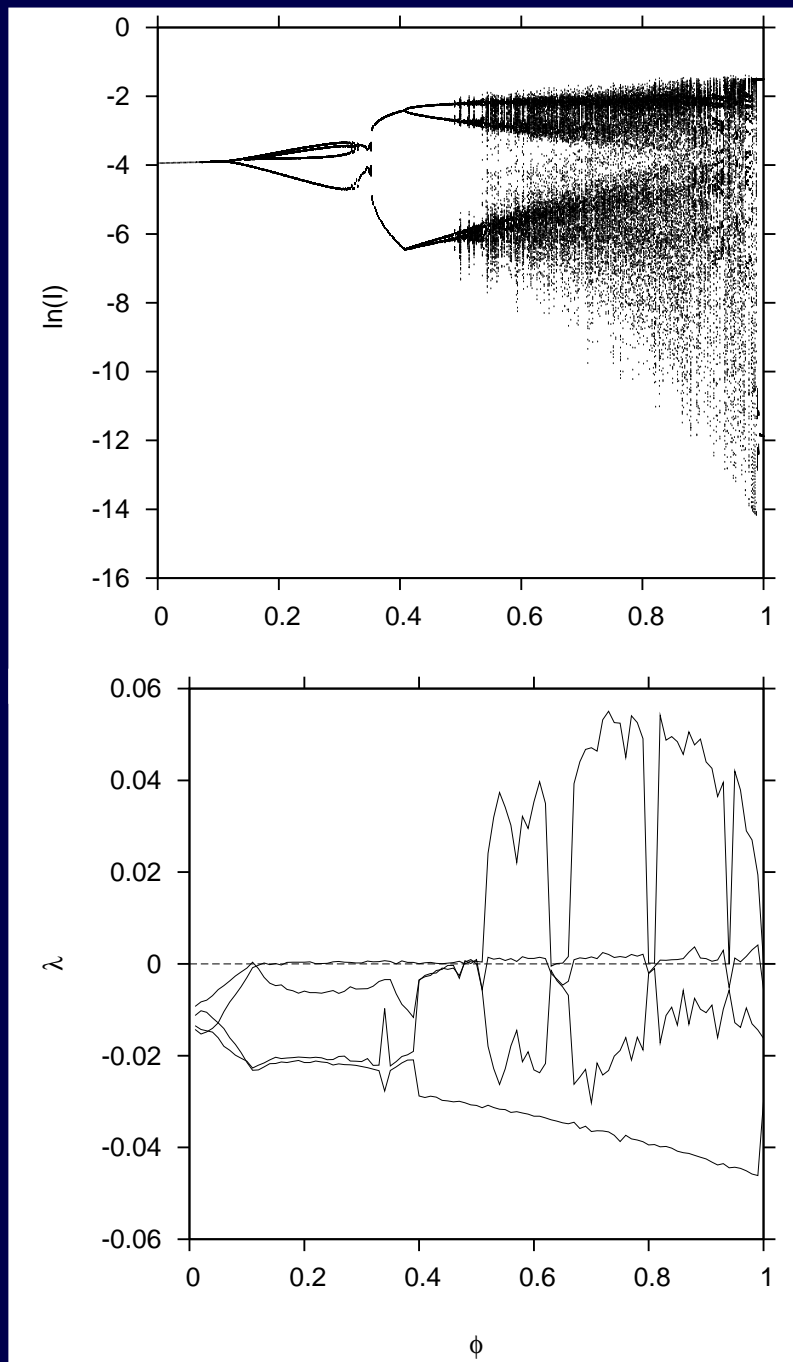
# Bifurcation diagram



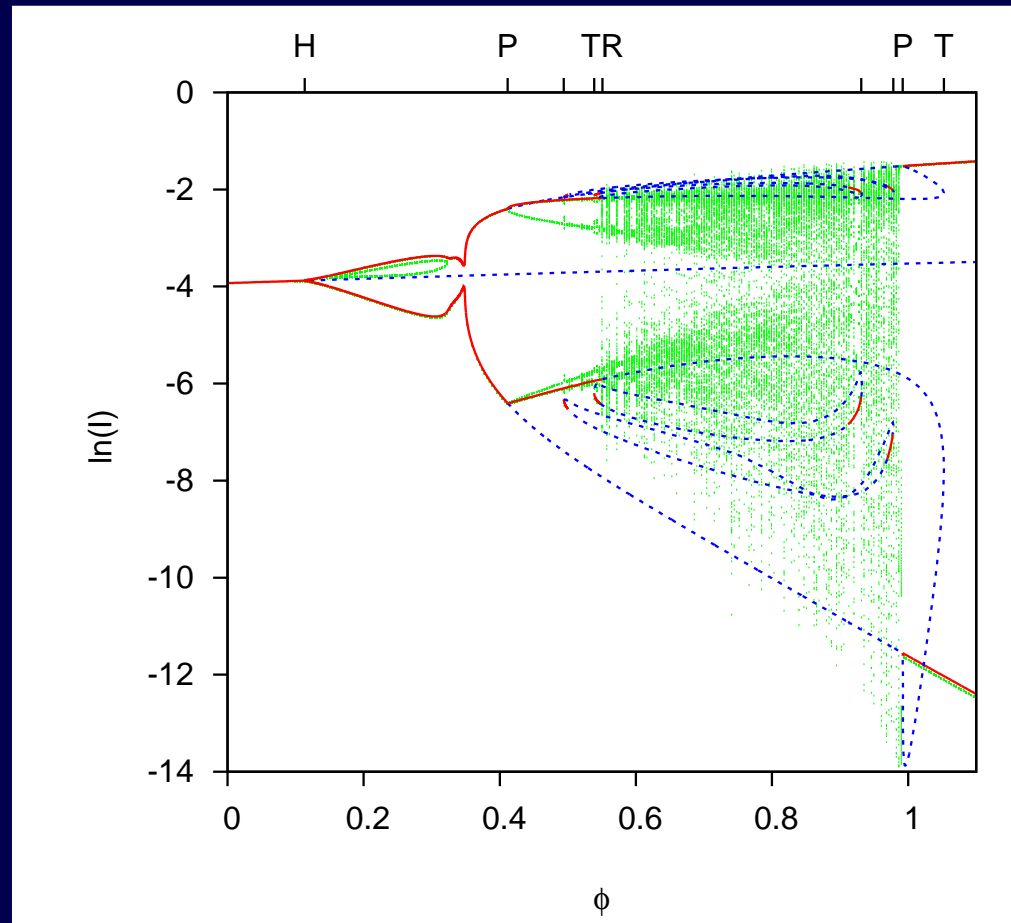
bifurcation diagram for  $\alpha = 2$   
i.e.  $\frac{1}{2}$  year of temporary cross-immunity



# Lyapunov spectrum versus bifurcation diagram



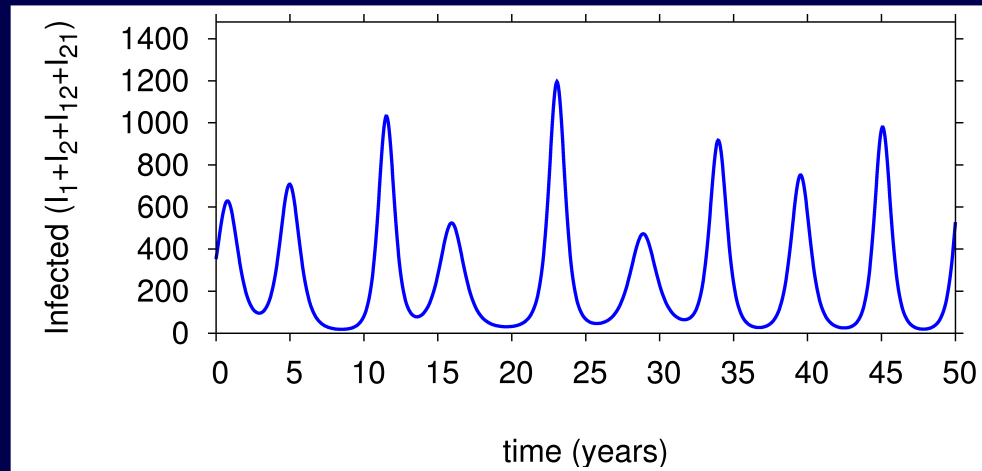
# Bifurcation analysis via continuation: AUTO



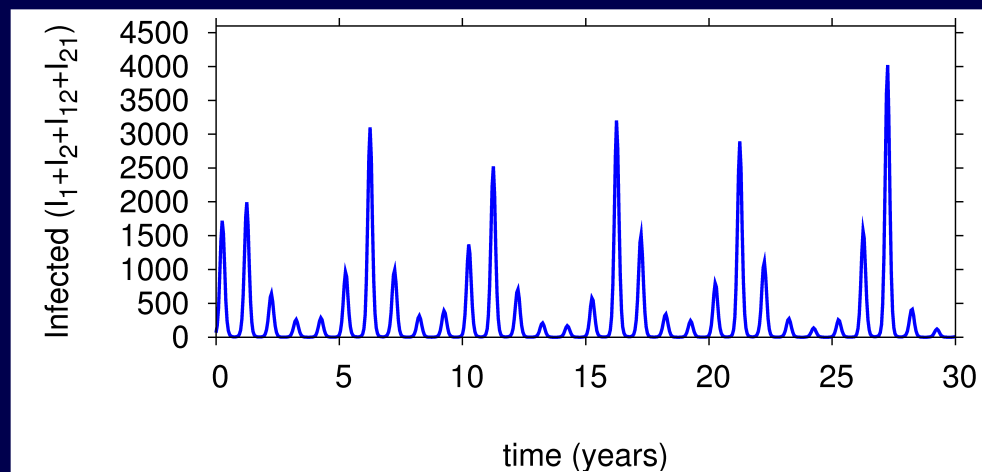
Comparing AUTO, Lyapunov spectra and  
numerical bifurcation diagrams:

coexisting attractors found, isolas

**Including seasonality**  
**gives time series comparable to data**

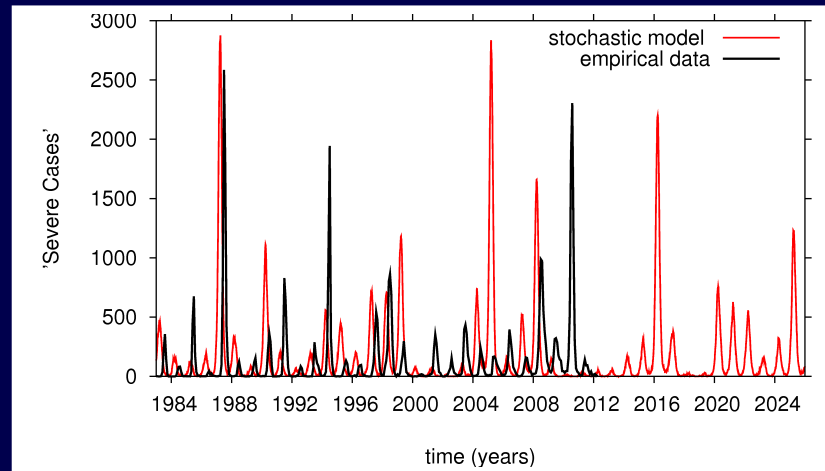


**non-seasonal model in chaotic region**

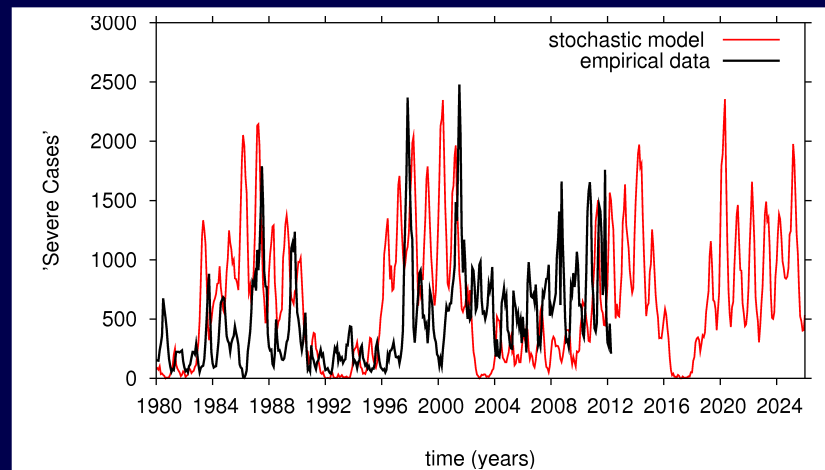


**seasonality preserves chaotic pattern**

# Data matching: compare simulations with data

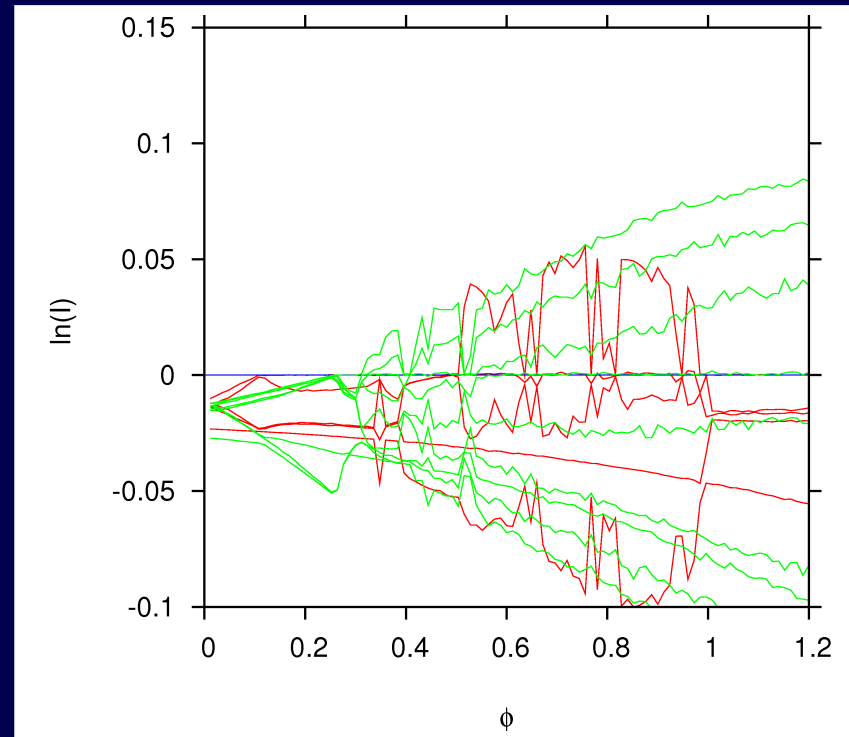
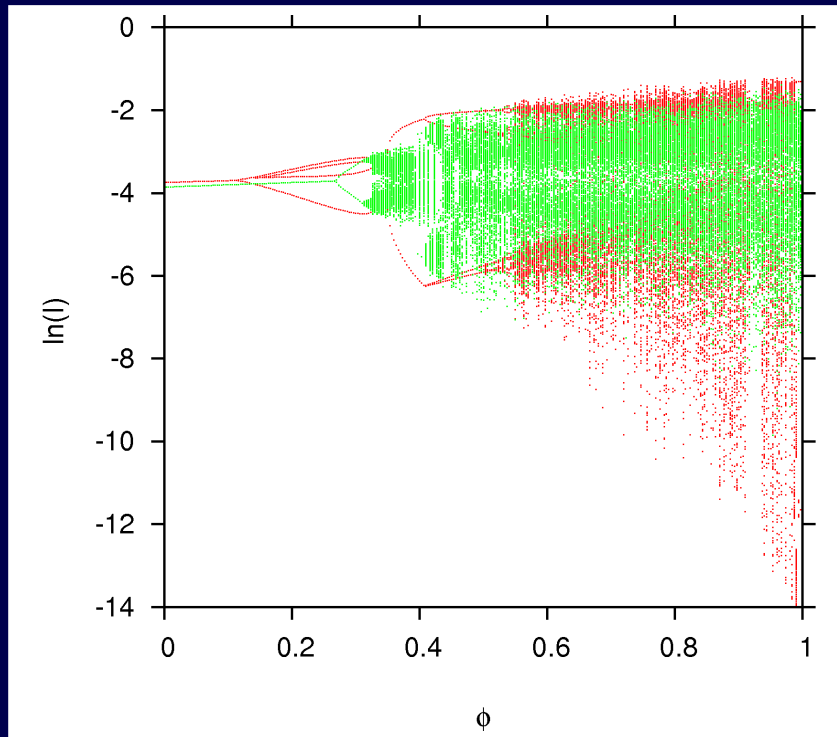


Chiang Mai



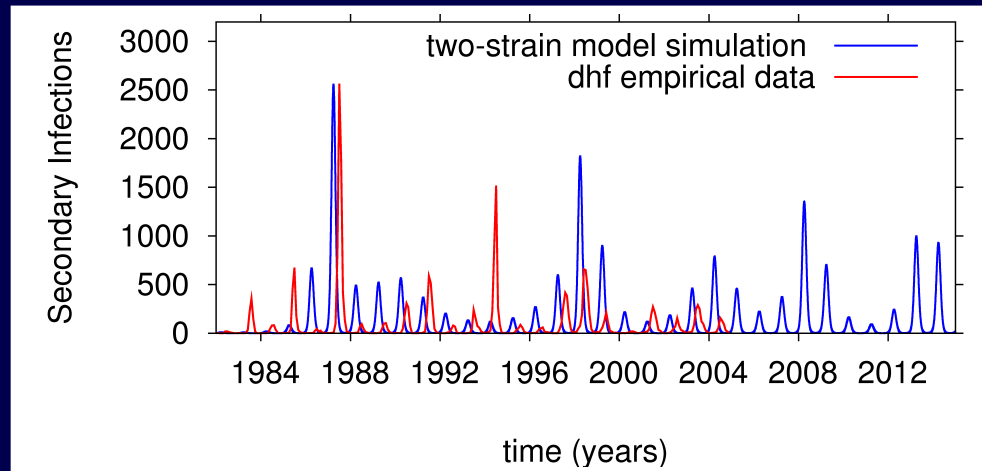
Krung Tep ("Bangkok")

# Comparing 2-strain with 4-strain models

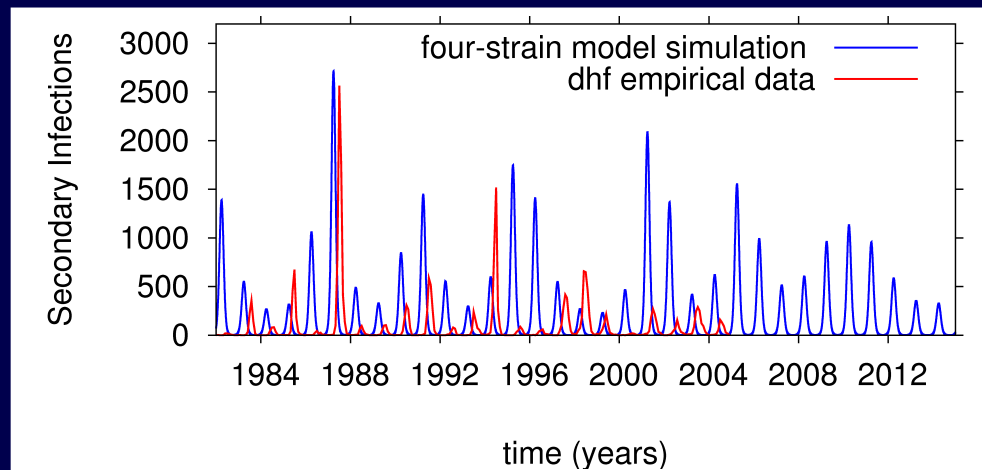


primary versus secondary infection drives the dynamics more than the exact number of strains

# Model comparison: 2-strain versus 4-strain models



## 2-strain model versus Chiang Mai data



## 4-strain model versus Chiang Mai data

European Union project  
**DENFREE: "Dengue reasearch Framework  
for Resisting Epidemics in Europe"**

DENFREE 

Dengue Research Framework For  
Resisting Epidemics In Europe  
Since-2012

**5 years project, start January 2012**

**together with 2 more EU project**

**"the largest financial effort on dengue research world wide"**

European Union project  
**DENFREE: "Dengue reasearch Framework  
for Resisting Epidemics in Europe"**

DENFREE 

Dengue Research Framework For  
Resisting Epidemics In Europe  
Since-2012

**5 years project, start January 2012**

**together with 2 more EU project**

**"the largest financial effort on dengue research world wide"**

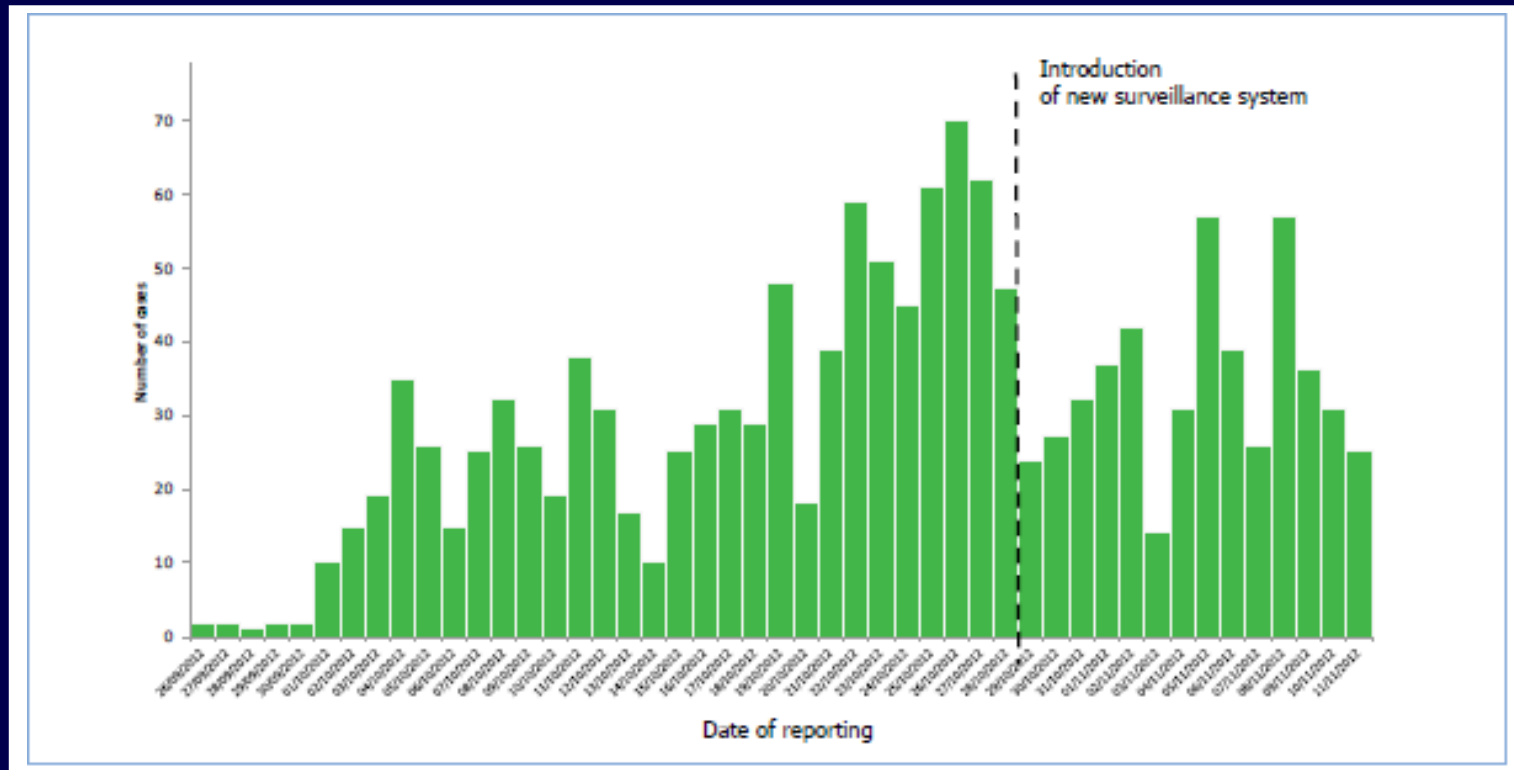
**CMAF is leading Work Package 4:**

**"Descriptic and predictive models for dengue fever"**



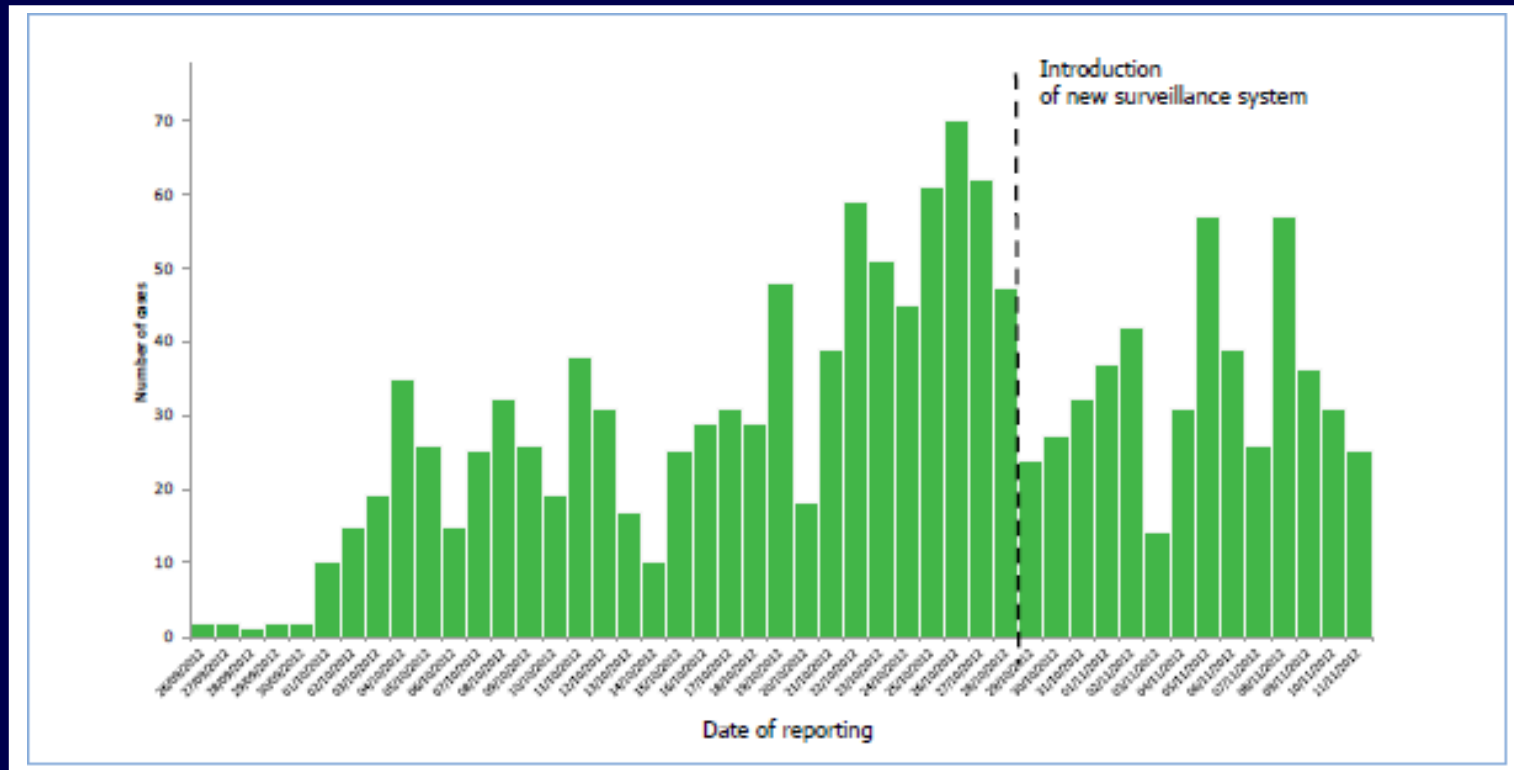
# Dengue fever outbreak on Madeira, Portugal, 2012

more than 2000 autochthonous cases detected



# Dengue fever outbreak on Madeira, Portugal, 2012

more than 2000 autochthonous cases detected



**European Center for Disease Control (ECDC):**  
"The largest dengue outbreak in Europe since the 1920th in Greece"

For data analysis:  
stochastic modelling

# Basic probability theory

joint probability

$$p(x, y)$$

marginal distribution

$$p(x) = \int p(x, y) dy$$

Bayes' rule

$$p(x, y) = p(x|y) \cdot p(y)$$

distribution that an event  $x_0$  is given with certainty is  $p(x) = \delta(x - x_0)$  with Dirac's delta-function

$$\int_a^b f(x) \cdot \delta(x - x_0) dx = f(x_0)$$

for  $x_0$  between  $a$  and  $b$

## Application to epidemic processes

joint probability to find  $I_{n+1}$  infected at time  $t + \Delta t$  and  $I_n$  at  $t$

$$p(I_{n+1}, I_n)$$

marginal distribution to find only one of the variables no matter what the other variable does

$$p(I_{n+1}) = \sum_{I_n=0}^N p(I_{n+1}, I_n)$$

Bayes' rule gives conditional probability  $p(I_{n+1}|I_n)$  for  $I_{n+1}$  knowing for sure  $I_n$  times  $p(I_n)$

$$p(I_{n+1}, I_n) = p(I_{n+1}|I_n) \cdot p(I_n)$$

giving a dynamic evolution equation for probabilities of infected  $p(I_n)$  at time  $t$  into  $p(I_{n+1})$  at time  $t + \Delta t$

$$p_{t+\Delta t}(I_{n+1}) = \sum_{I_n=0}^N p(I_{n+1}|I_n) \cdot p_t(I_n)$$

# Application to epidemic processes

equation

$$p_{t+\Delta t}(I_{n+1}) = \sum_{I_n=0}^N p(I_{n+1}|I_n) \cdot p_t(I_n)$$

is a Perron-Frobenius type equation, and defines a time discrete Markov process

## Application to epidemic processes

differential quotient gives time continuous Markov process

$$\frac{p_{t+\Delta t}(I) - p_t(I)}{\Delta t} \approx \frac{d}{dt} p(I)$$

hence inserting time discrete version with  $I := I_{n+1}$  and  $\tilde{I} := I_n$

$$\frac{p_{t+\Delta t}(I) - p_t(I)}{\Delta t} = \sum_{\tilde{I}=0}^N \left( \frac{1}{\Delta t} p(I|\tilde{I}) \right) p_t(\tilde{I}) - \frac{1}{\Delta t} p_t(I)$$

and inserting normalization of conditioned probability  $\sum_{\tilde{I}=0}^N p(\tilde{I}|I) = 1$  into the last term gives

$$\frac{d}{dt} p(I) = \sum_{\tilde{I}=0}^N w_{I|\tilde{I}} p_t(\tilde{I}) - \sum_{\tilde{I}=0}^N w_{\tilde{I}|I} p_t(I)$$

with transition rates  $w_{I|\tilde{I}} := \left( \frac{1}{\Delta t} p(I|\tilde{I}) \right)$

# Application to epidemic processes

equation

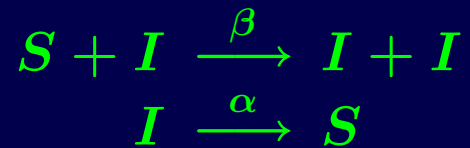
$$\frac{d}{dt} p(I) = \sum_{\tilde{I}=0, \tilde{I} \neq I}^N w_{I|\tilde{I}} p_t(\tilde{I}) - \sum_{\tilde{I}=0, \tilde{I} \neq I}^N w_{\tilde{I}|I} p_t(I)$$

is also called master equation and defines a time continuous state discrete Markov process



# SIS epidemic

stochastic process



for variable  $I$  and  $S = N - I \quad \Rightarrow \quad$  probab.  $p(I, t)$

$$\begin{aligned} \frac{d}{dt} p(I, t) &= \frac{\beta}{N} (I - 1)(N - (I - 1)) p(I - 1, t) + \alpha (I + 1) p(I + 1, t) \\ &\quad - \left( \frac{\beta}{N} I(N - I) + \alpha I \right) p(I, t) \end{aligned}$$

$$\text{mean } \langle I \rangle := \sum_{I=0}^N I \cdot p(I, t)$$

$$\frac{d}{dt} \langle I \rangle = (\beta - \alpha) \langle I \rangle - \frac{\beta}{N} \langle I^2 \rangle$$

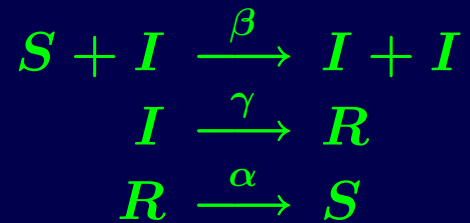
and only in mean field approx.  $var := \langle I^2 \rangle - \langle I \rangle^2 \approx 0$

$$\frac{d}{dt} \langle I \rangle = \frac{\beta}{N} \langle I \rangle (N - \langle I \rangle) - \alpha \langle I \rangle$$

we obtain closed ODE

# SIR epidemic

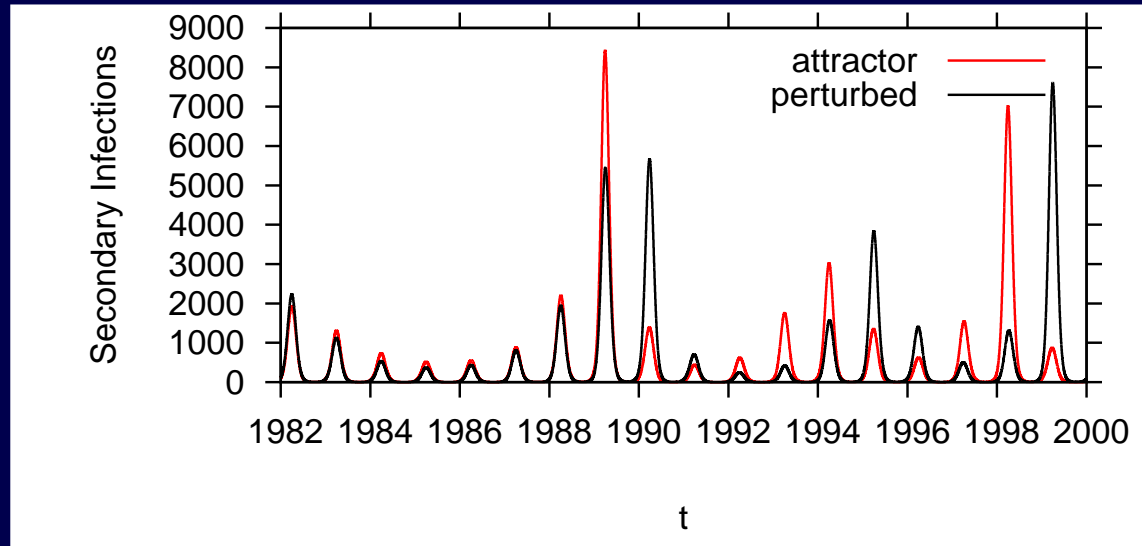
stochastic process



for variables  $S$ ,  $I$  and  $R = N - S - I \Rightarrow$  probab.  
 $p(S, I, t)$

$$\begin{aligned} \frac{d}{dt} p(S, I, t) &= \frac{\beta}{N} (I - 1)(S + 1) p(S + 1, I - 1, t) \\ &\quad + \gamma (I + 1) p(S, I + 1, t) \\ &\quad + \alpha (N - (S + 1) - I) p(S + 1, I, t) \\ &\quad - \left( \frac{\beta}{N} SI + \gamma I + \alpha (N - S - I) \right) p(S, I, t) \end{aligned}$$

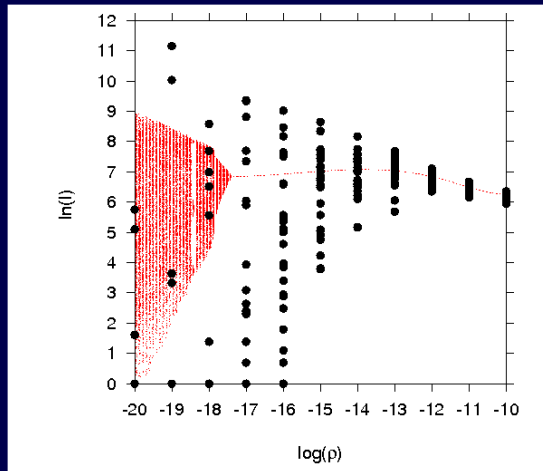
# Short term predictability, long term unpredictability



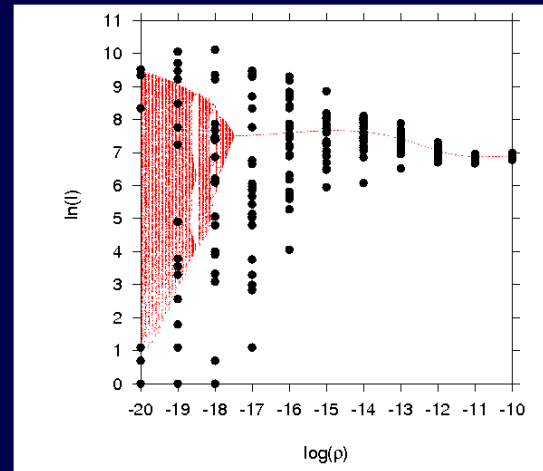
simulations with different initial conditions

implications for data analysis: Maximum Likelihood Iterated Filtering (MIF) is choice for such systems (Ionides et al 2006/ Bretó et al. 2009)

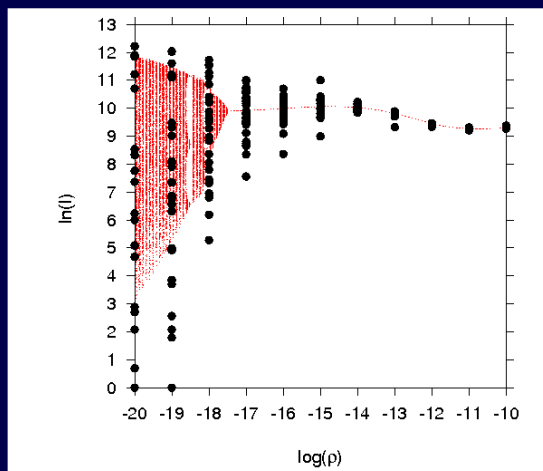
# Parameter estimation in dengue: scaling with noise, importance of import



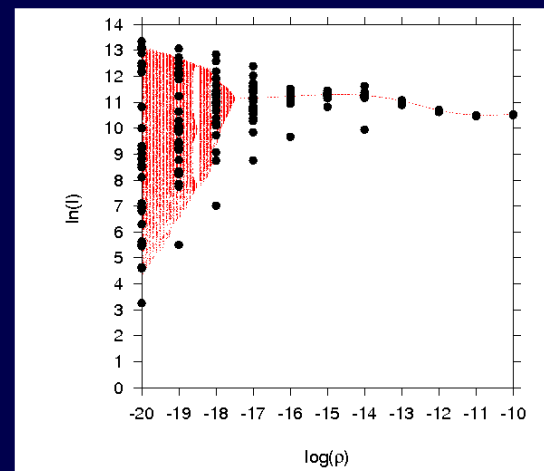
Chiang Mai  
 $N \approx 1$  mio.



North  
 $N \approx 6$  mio



Thailand  
 $N \approx 60$  mio.

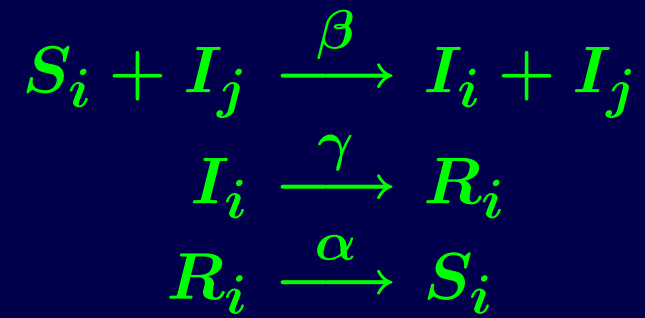


South East Asia  
 $N \approx 250$  mio

# Individual based models

# Individual based models

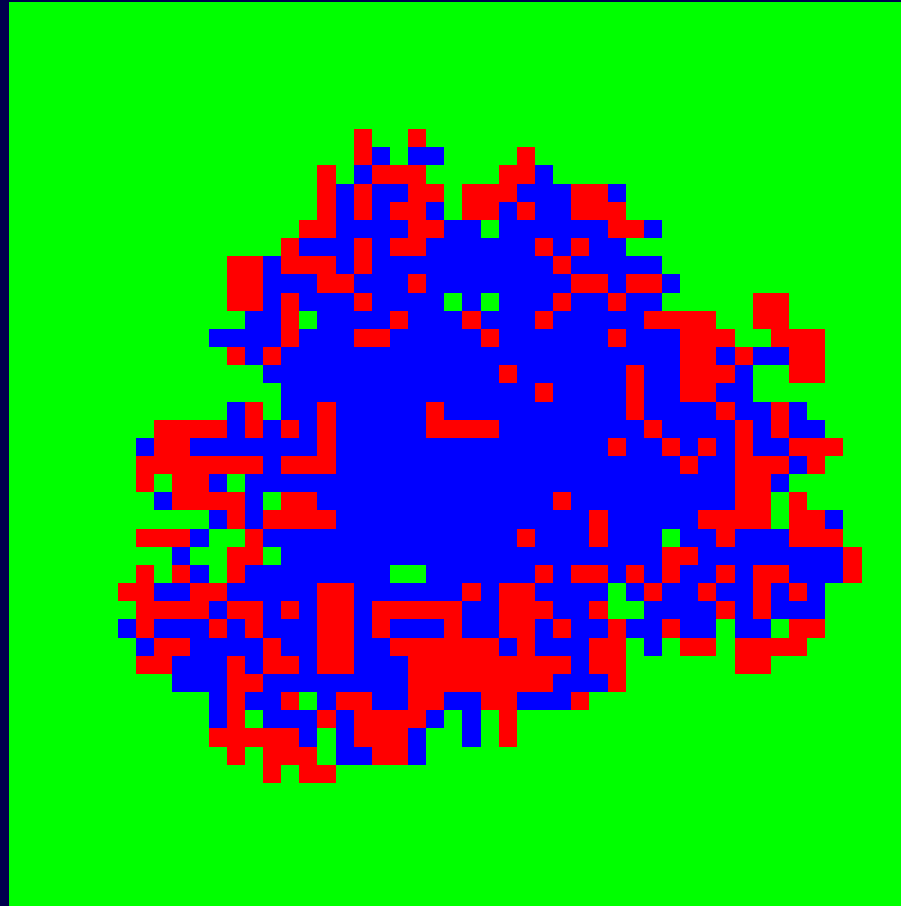
## basic epidemic model: SIR



# Individual based models

example: stochastic 2 dimensional SIR epidemic

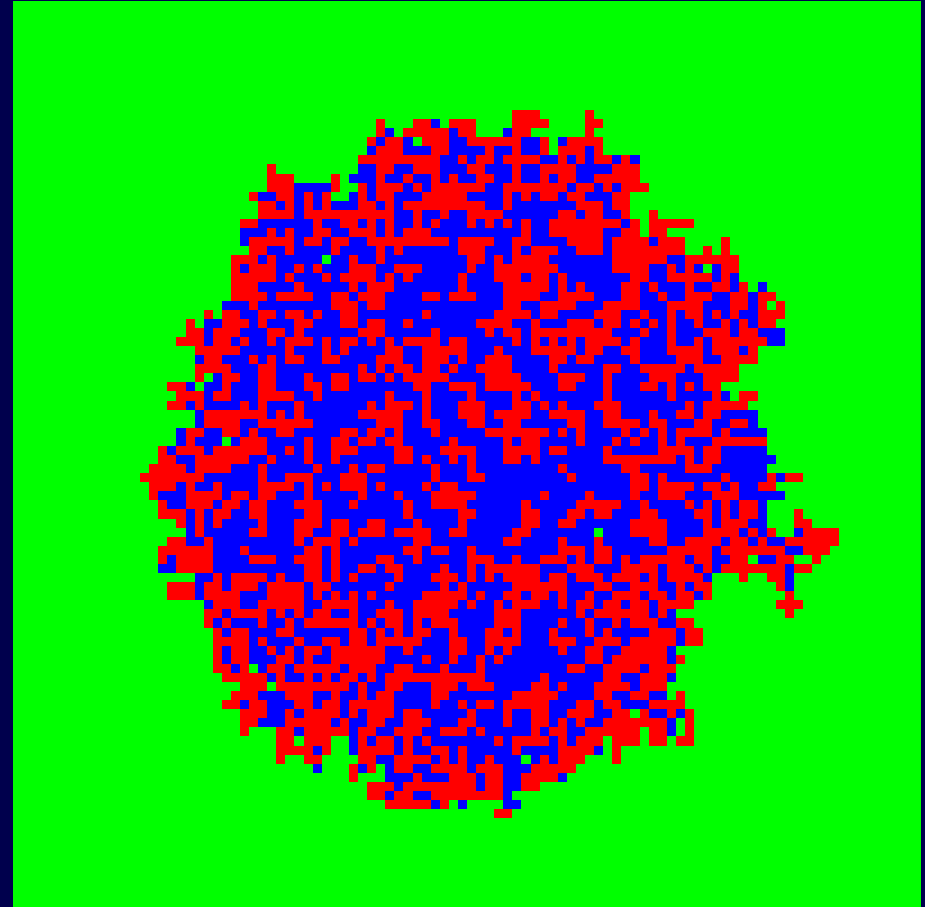
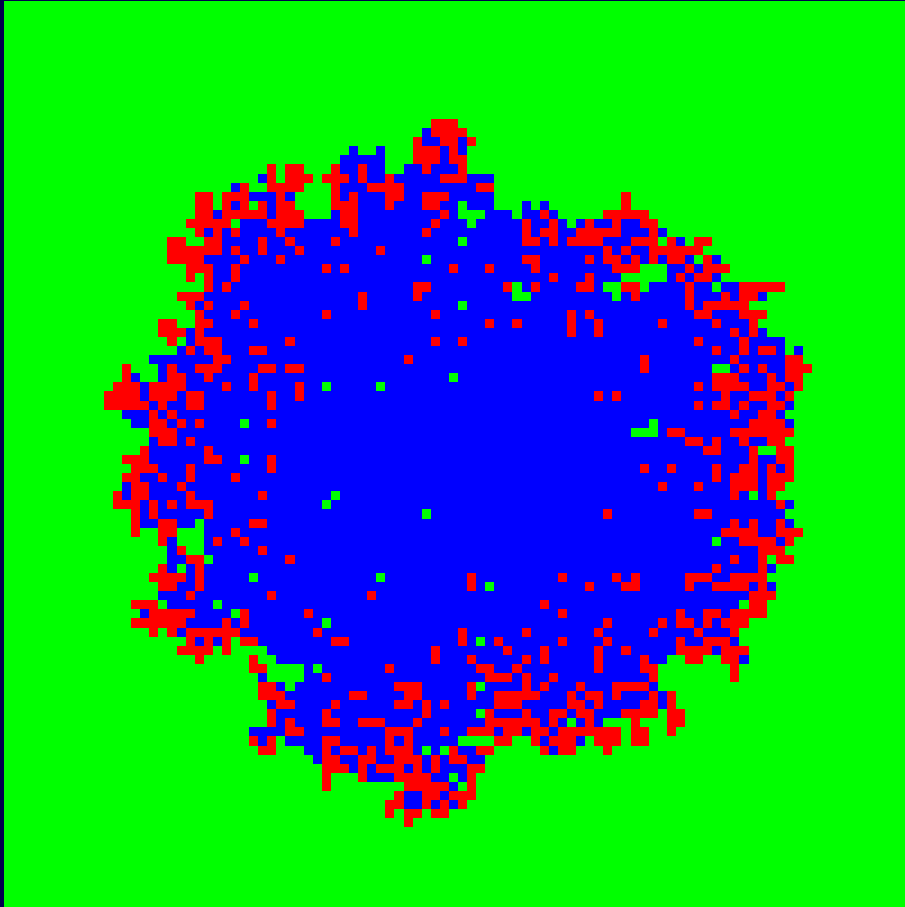
S green, I red, R blue



# Individual based models

example: stochastic 2 dimensional SIRI epidemic

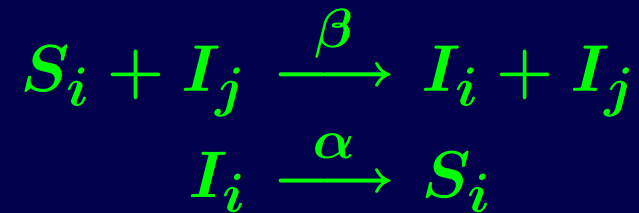
S green, I red, R blue





## Master equation for spatial SIS model

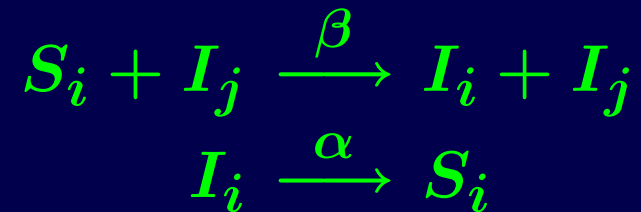
consider as example again SIS epidemic model



now at lattice site  $i \in \{1, \dots, N\}$  an infected  $I_i = 1$ , or not  $I_i = 0$  hence  $S_i := 1 - I_i = 1$ , stochastic dynamics now given for variable  $I_i \in \{0, 1\}$

## Master equation for spatial SIS model

consider as example again SIS epidemic model



now at lattice site  $i \in \{1, \dots, N\}$  an infected  $I_i = 1$ , or not  $I_i = 0$  hence  $S_i := 1 - I_i = 1$ , stochastic dynamics now given for variable  $I_i \in \{0, 1\}$

stochastic dynamics now given for variables  $I_i \in \{0, 1\}$  for  $i \in \{1, \dots, N\}$

## Master equation for spatial SIS model

stochastic dynamics now given for variables  $I_i \in \{0, 1\}$   
for  $i \in \{1, \dots, N\}$

$$\begin{aligned} \frac{d}{dt} p(I_1, I_2, \dots, I_N, t) &= \sum_{i=1}^N \beta \left( \sum_{j=1}^N J_{ij} I_j \right) I_i p(I_1, \dots, 1 - I_i, \dots, I_N, t) \\ &\quad + \sum_{i=1}^N \alpha (1 - I_i) p(I_1, \dots, 1 - I_i, \dots, I_N, t) \\ &\quad - \sum_{i=1}^N \left[ \beta \left( \sum_{j=1}^N J_{ij} I_j \right) (1 - I_i) + \alpha I_i \right] p(I_1, \dots, I_i, \dots, I_N, t) \end{aligned}$$

with adjacency matrix  $J_{ij} \in \{0, 1\}$

# Clusters and their dynamics

total number of infected individuals on the lattices

$$[I] := \sum_{i=1}^N I_i$$

total number of susceptibles

$$[S] := \sum_{i=1}^N (1 - I_i)$$

total number of pairs

$$[II] := \sum_{i=1}^N \sum_{j=1}^N J_{ij} I_i \cdot I_j$$

triples

$$[III] := \sum_{i=1}^N \sum_{j=1}^N \sum_{k=1}^N J_{ij} J_{jk} \cdot I_i I_j I_k$$

# Clusters and their dynamics

triangles

$$[\Delta] := \sum_{i=1}^N \sum_{j=1}^N \sum_{k=1}^N J_{ij} J_{jk} J_{ki} \cdot I_i I_j I_k$$

space averages, e.g.  $[I] := \sum_{i=1}^N I_i$ , depend on the ensemble  $(I_1, \dots, I_N)$ , hence define ensemble average

$$\langle I \rangle(t) := \sum_{I_1=0}^1 \dots \sum_{I_N=0}^1 [I] p(I_1, \dots, I_N, t)$$

and generally for any function  $f = f(I_1, \dots, I_N)$

$$\langle f \rangle(t) := \sum_{I_1=0}^1 \dots \sum_{I_N=0}^1 f(I_1, \dots, I_N) p(I_1, \dots, I_N, t)$$

then time evolution to calculate from master equation

$$\frac{d}{dt} \langle f \rangle(t) := \sum_{I_1=0}^1 \dots \sum_{I_N=0}^1 f(I_1, \dots, I_N) \frac{d}{dt} p(I_1, \dots, I_N, t)$$

# Dynamics of expectation values in spatial systems

## local mean value dynamics

$$\begin{aligned}\frac{d}{dt} \langle I_i \rangle &:= \sum_{I_1=0}^1 \dots \sum_{I_N=0}^1 I_i \frac{d}{dt} p(I_1, \dots, I_N, t) \\ &= \dots \\ &= \beta \sum_{j=1}^N J_{ij} \langle I_j (1 - I_i) \rangle - \alpha \langle I_i \rangle \\ &= \beta \sum_{j=1}^N J_{ij} \langle S_i I_j \rangle - \alpha \langle I_i \rangle\end{aligned}$$

# Dynamics of expectation values in spatial systems

global mean value dynamics

$$\begin{aligned}\frac{d}{dt} \langle I \rangle &= \sum_{i=1}^N \frac{d}{dt} \langle I_i \rangle \\ &= b \left( Q \langle I \rangle - \langle II \rangle_1 \right) - a \langle I \rangle \\ &= b \langle SI \rangle_1 - a \langle I \rangle\end{aligned}$$

using  $Q_i := \sum_{j=1}^N J_{ij}$  number of sites connected to site  $i$ , and for regular lattices  $Q_i = Q$  constant

# Dynamics of expectation values in spatial systems

global mean value dynamics

$$\begin{aligned}\frac{d}{dt} \langle I \rangle &= b \left( Q \langle I \rangle - \langle II \rangle_1 \right) - a \langle I \rangle \\ &= b \langle SI \rangle_1 - a \langle I \rangle\end{aligned}$$

contains pair expectations  $\langle II \rangle_1 = \sum_{i=1}^N \sum_{j=1}^N J_{ij} \langle I_i I_j \rangle$   
hence to calculate dynamics for pairs

$$\frac{d}{dt} \langle II \rangle_1 = \sum_{i=1}^N \sum_{j=1}^N J_{ij} \frac{d}{dt} \langle I_i I_j \rangle$$

giving

$$\begin{aligned}\frac{d}{dt} \langle II \rangle_1 &= 2b \left( \langle II \rangle_2 - \langle III \rangle_{1,1} \right) - 2a \langle II \rangle_1 \\ &= 2b \langle ISI \rangle_{1,1} - 2a \langle II \rangle_1\end{aligned}$$



# Dynamics of expectation values in spatial systems

dynamics for pairs

$$\begin{aligned}\frac{d}{dt} \langle II \rangle_1 &= 2b \left( \langle II \rangle_2 - \langle III \rangle_{1,1} \right) - 2a \langle II \rangle_1 \\ &= 2b \langle ISI \rangle_{1,1} - 2a \langle II \rangle_1\end{aligned}$$

now includes triples

$$\langle ISI \rangle_{1,1} := \sum_{i=1}^N \sum_{j=1}^N \sum_{k=1}^N J_{ij}^1 J_{jk}^1 \langle I_i (1 - I_j) I_k \rangle$$

or longer range correlations

$$\langle II \rangle_2 := \sum_{i=1}^N \sum_{k=1}^N \underbrace{\left( \sum_{j=1}^N J_{ij} J_{jk} \right)}_{=:(J^2)_{ik}} \langle I_i I_k \rangle$$

## Approximating pairs

global mean value dynamics contains pairs

$$\frac{d}{dt} \langle I \rangle = b \left( Q \langle I \rangle - \langle II \rangle_1 \right) - a \langle I \rangle$$

which can be approximated by an interaction of  $I_i$  not with its neighbours  $I_j$  but with an average of all other sites  $\langle I \rangle$

$$\sum_{j=1}^N J_{kj} I_j \approx \sum_{j=1}^N J_{kj} \frac{\langle I \rangle}{N}$$

called "interacting with a mean field" instead of its neighbours directly

## Approximating pairs

global mean value dynamics contains pairs

$$\frac{d}{dt} \langle I \rangle = b \left( Q \langle I \rangle - \langle II \rangle_1 \right) - a \langle I \rangle$$

which can be approximated by an interaction of  $I_i$  not with its neighbours  $I_j$  but with an average of all other sites  $\langle I \rangle$

$$\sum_{j=1}^N J_{kj} I_j \approx \sum_{j=1}^N J_{kj} \frac{\langle I \rangle}{N}$$

called "interacting with a mean field" instead of its neighbours directly, hence

mean field approximation

# Mean field approximation

technically

$$\begin{aligned}\langle II \rangle_1 &= \left\langle \sum_{i=1}^N \sum_{j=1}^N J_{ij} I_i I_j \right\rangle = \left\langle \sum_{i=1}^N I_i \sum_{j=1}^N J_{ij} I_j \right\rangle \\ &\approx \left\langle \sum_{i=1}^N I_i \frac{Q}{N} \cdot \langle I \rangle \right\rangle = \frac{Q}{N} \cdot \langle I \rangle \cdot \left\langle \sum_{i=1}^N I_i \right\rangle \\ &= \frac{Q}{N} \cdot \langle I \rangle^2\end{aligned}$$

giving in the dynamics of the mean a closed ODE

$$\begin{aligned}\frac{d}{dt} \langle I \rangle &= b \left( Q \langle I \rangle - \frac{Q}{N} \langle I \rangle^2 \right) - a \langle I \rangle \\ &= \frac{bQ}{N} \langle I \rangle (N - \langle I \rangle) - a \langle I \rangle\end{aligned}$$

# Mean field approximation

technically

$$\begin{aligned}\langle II \rangle_1 &= \left\langle \sum_{i=1}^N \sum_{j=1}^N J_{ij} I_i I_j \right\rangle = \left\langle \sum_{i=1}^N I_i \sum_{j=1}^N J_{ij} I_j \right\rangle \\ &\approx \left\langle \sum_{i=1}^N I_i \frac{Q}{N} \cdot \langle I \rangle \right\rangle = \frac{Q}{N} \cdot \langle I \rangle \cdot \left\langle \sum_{i=1}^N I_i \right\rangle \\ &= \frac{Q}{N} \cdot \langle I \rangle^2\end{aligned}$$

giving in the dynamics of the mean a closed ODE

$$\begin{aligned}\frac{d}{dt} \langle I \rangle &= b \left( Q \langle I \rangle - \frac{Q}{N} \langle I \rangle^2 \right) - a \langle I \rangle \\ &= \frac{bQ}{N} \langle I \rangle (N - \langle I \rangle) - a \langle I \rangle\end{aligned}$$

our famous ODE of the SIS system from before  
with  $\beta = bQ$

## Approximating triples into pairs

global dynamics dynamics contains triples

$$\begin{aligned}\frac{d}{dt} \langle II \rangle_1 &= 2b \left( \langle II \rangle_2 - \langle III \rangle_{1,1} \right) - 2a \langle II \rangle_1 \\ &= 2b \langle ISI \rangle_{1,1} - 2a \langle II \rangle_1\end{aligned}$$

idea of approximation

$$\langle SIR \rangle \approx \frac{\langle SI \rangle \cdot \langle IR \rangle}{\langle I \rangle}$$

is basically a Bayes' rule now for conditioned mean

values  $\langle I_i | I_j \rangle := \sum_{I_i=0}^1 I_i p(I_i | I_j)$ , namely

$$\langle I_i I_j \rangle = \langle I_i | I_j = 1 \rangle \cdot \langle I_j \rangle$$

respectively for triples

$$\langle I_i I_j I_k \rangle = \langle I_i | I_j = 1, I_k = 1 \rangle \cdot \langle I_j I_k \rangle$$

## Approximating triples into pairs

essential approximation: the mean at location  $i$  depends on its neighbour  $j$ , but not on the next neighbour  $k$

$$\langle I_i | I_j = 1, I_k = 1 \rangle \approx \langle I_i | I_j = 1 \rangle$$

giving

$$\langle I_i I_j I_k \rangle \approx \frac{\langle I_i I_j \rangle}{\langle I_j \rangle} \cdot \langle I_j I_k \rangle$$

and then to pull up to global quantities

# Dynamics in pair approximation

from the original system

$$\frac{d}{dt}\langle I \rangle = b(Q\langle I \rangle - \langle II \rangle_1) - a\langle I \rangle$$

$$\frac{d}{dt}\langle II \rangle_1 = 2b\left(\langle II \rangle_2 - \langle III \rangle_{1,1}\right) - 2a\langle II \rangle_1$$

in pair approximation we obtain for densities

$$x := \langle I \rangle / N \in [0, 1]$$

$$y := \langle II \rangle_1 / (NQ) \in [0, 1]$$

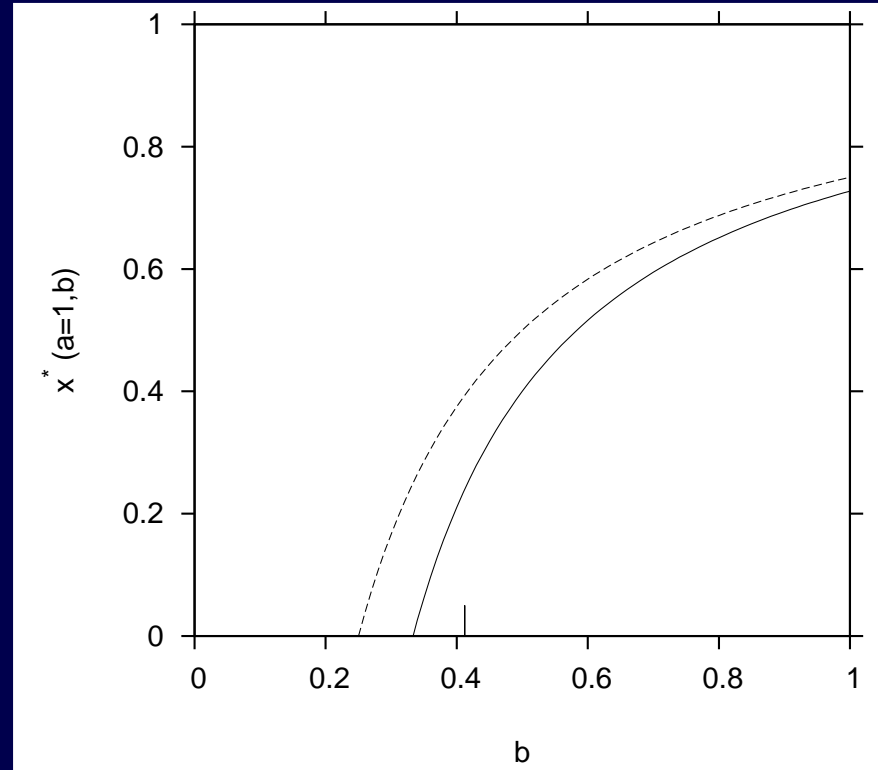
the closed ODE system

$$\frac{dx}{dt} = bQ(x - y) - ax$$

$$\frac{dy}{dt} = 2b(Q - 1)\frac{(x - y)^2}{1 - x} + 2b(x - y) - 2ay$$

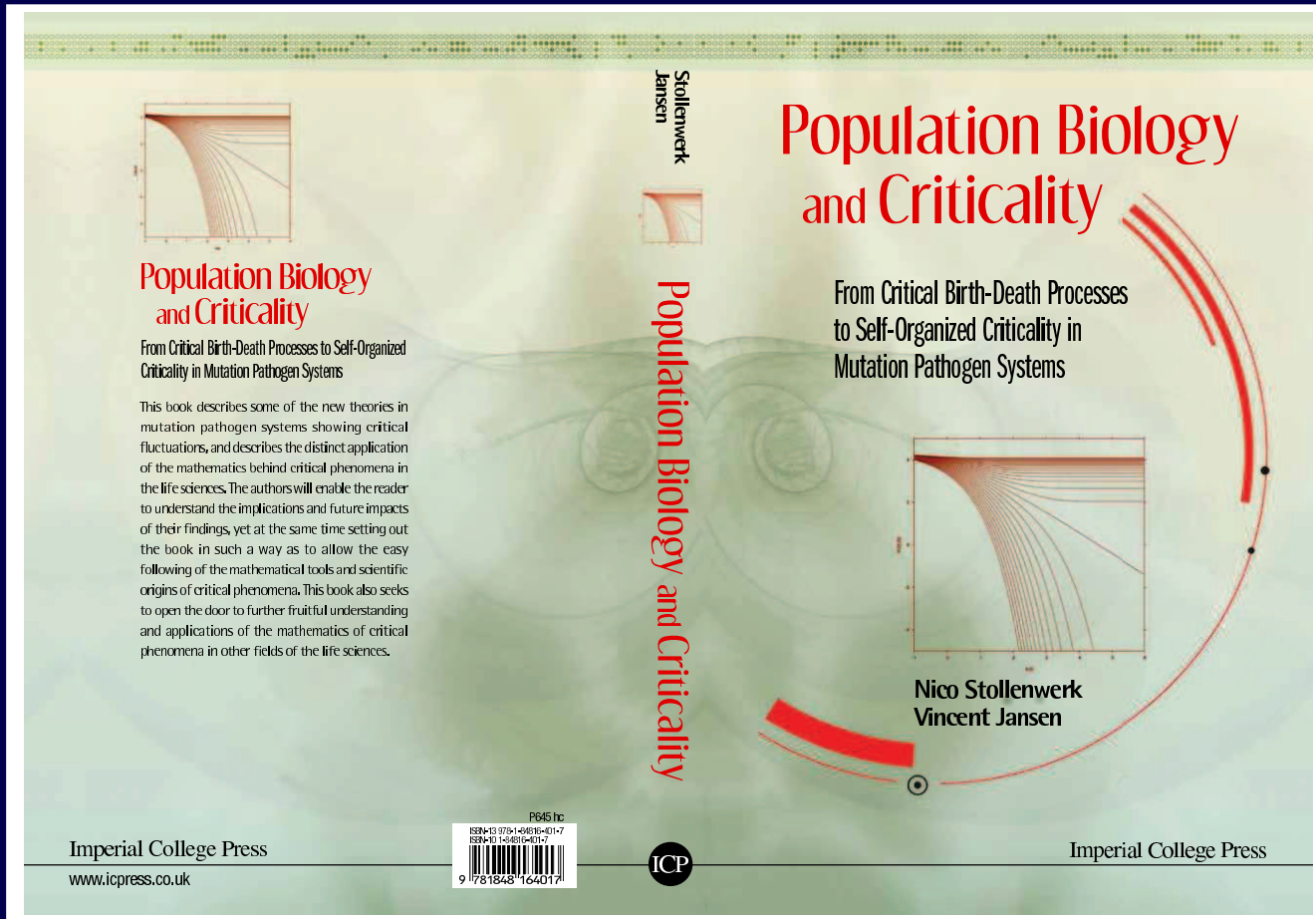


# Dynamics in pair approximation



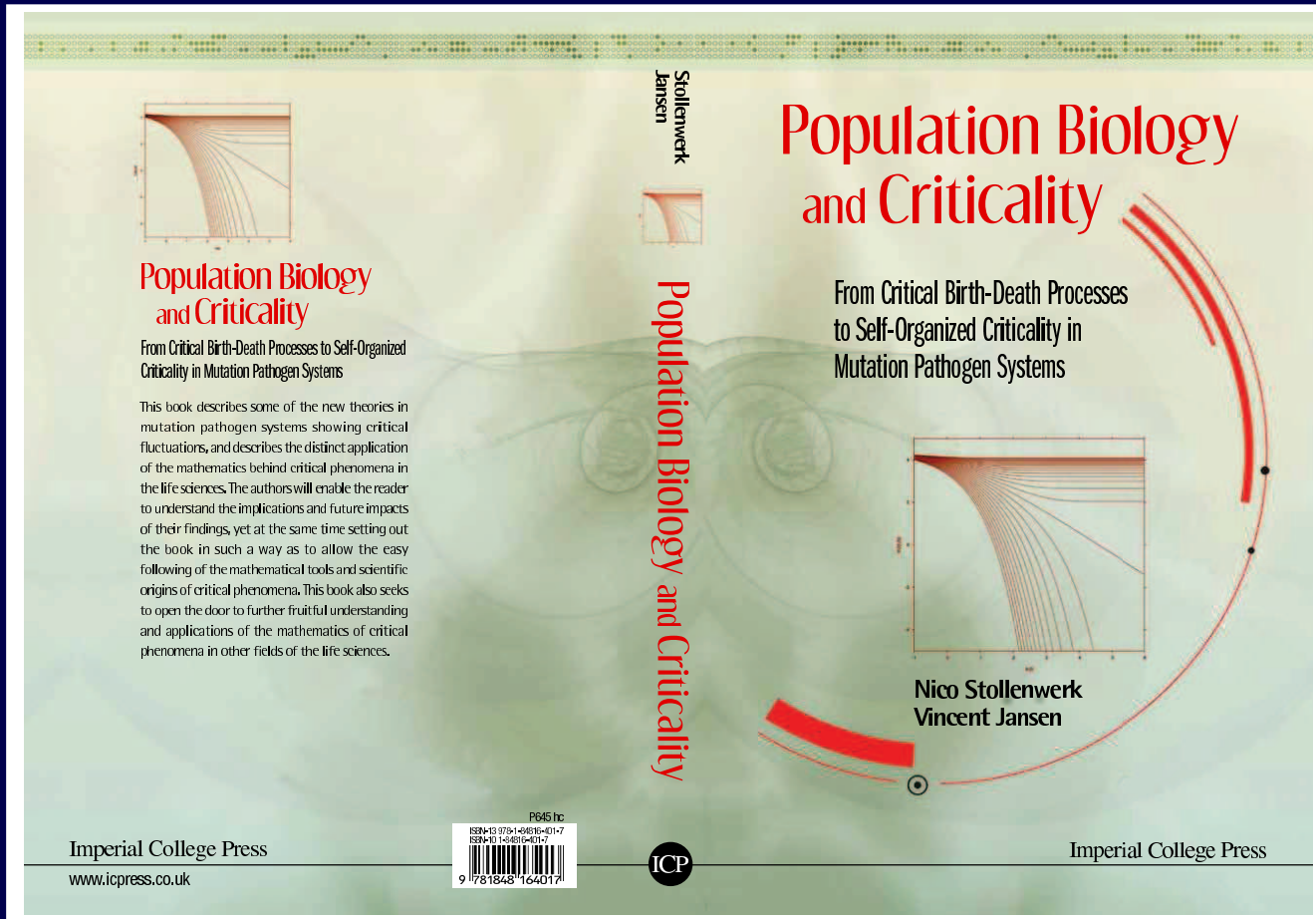
mean field, pair approximation, spatial simulation  
(from left to right)

# Theory of accidental pathogens, paradigmatic system: bacterial meningitis



in many-strain systems with fast evolution  
evolution towards critical fluctuations (SOC :-)

# Theory of accidental pathogens, paradigmatic system: bacterial meningitis



Muñoz et al. (2011): the "Stollenwerk-Jansen model (SJ)"  
is in universality class of voter model

# Dynamics of expectation values in spatial systems

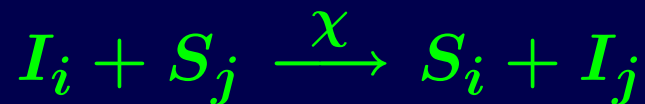
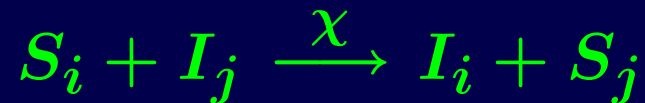
## local mean value dynamics

$$\begin{aligned}\frac{d}{dt} \langle I_i \rangle &:= \sum_{I_1=0}^1 \dots \sum_{I_N=0}^1 I_i \frac{d}{dt} p(I_1, \dots, I_N, t) \\ &= \dots \\ &= \beta \sum_{j=1}^N J_{ij} \langle I_j (1 - I_i) \rangle - \alpha \langle I_i \rangle \\ &= \beta \sum_{j=1}^N J_{ij} \langle S_i I_j \rangle - \alpha \langle I_i \rangle\end{aligned}$$

Surrogate for human contact dynamics:

exchanging money :-)

reaction scheme for exchanging an item from item holder  $I_i$  to susceptible  $S_j$  to receive this item



gives dynamics of local expectation value

$$\frac{d}{dt} \langle I_i \rangle = \chi \sum_{j=1}^N J_{ij} (\langle I_j \rangle - \langle I_i \rangle) =: \chi \cdot \Delta \langle I_i \rangle$$

diffusion equation for regular lattices, generalizable to contact probabilities proportional to distance of individuals

”spatially restricted networks”

# Surrogate for human contact dynamics:

exchanging money :-)

superdiffusion via fractional Laplace operator for  $\mu \leq 2$

$$\frac{\partial}{\partial t} u(x, t) = \chi \frac{\partial^\mu}{\partial x^\mu} u(x, t)$$

defined via the Fourier transform (Riesz fractional derivative)  $\frac{\partial^\mu}{\partial x^\mu} e^{ikx} := -|k|^\mu \cdot e^{ikx}$  in

$$\frac{\partial}{\partial t} u(x, t) = \chi \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{\infty} \tilde{u}(k, t) \left( \frac{\partial^\mu}{\partial x^\mu} e^{ikx} \right) dk$$

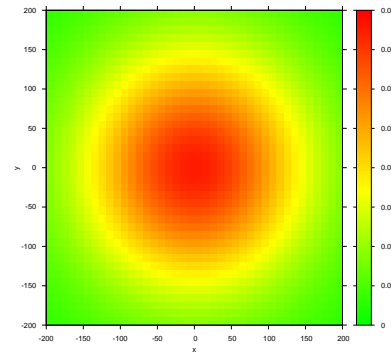
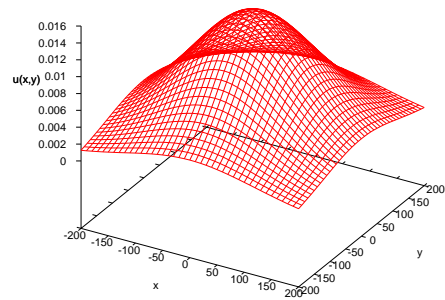
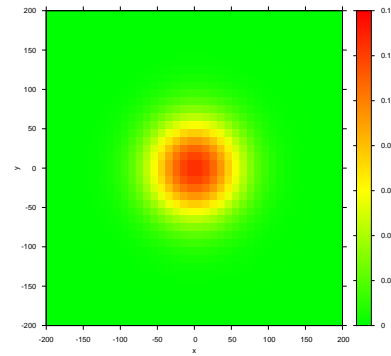
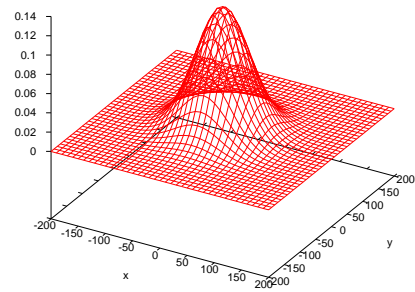
using convolution and with constant

$$c_\mu := \frac{1}{\pi} \Gamma(\mu + 1) \sin\left(\frac{\pi}{2}\mu\right)$$

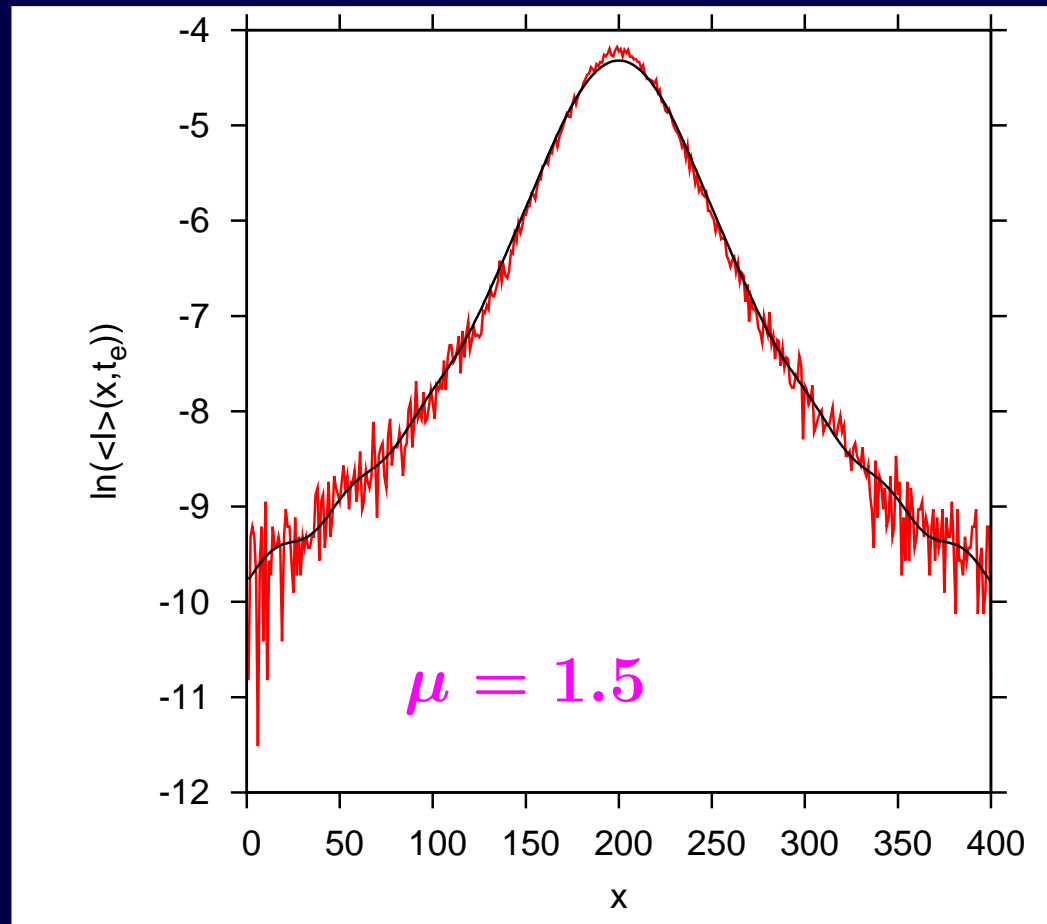
$$\frac{\partial}{\partial t} u(x, t) = (\chi \cdot c_\mu) \int_{-\infty}^{\infty} \frac{u(y, t)}{|x - y|^{\mu+1}} dy$$

as integral representation of superdiffusive Laplace

# Super-diffusion in higher dimensions



# Spatial spreading in epidemiological systems: Superdiffusion using fractional calculus



stochastic histogram and fractional diffusion equation

$$\langle I_i \rangle \approx u(\underline{x}_i, t)$$

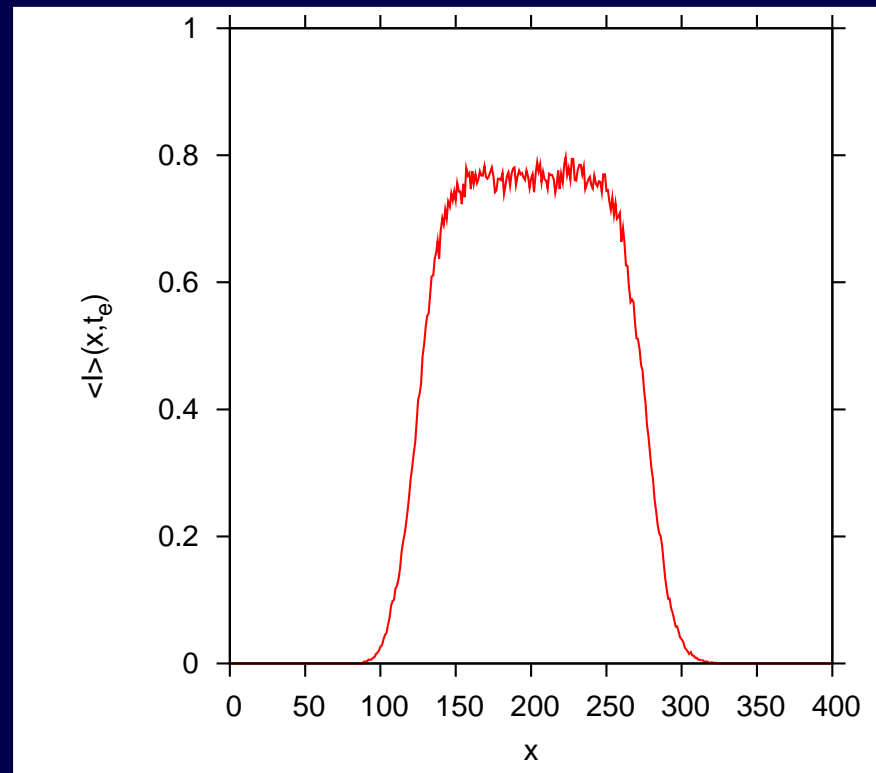


# Reaction-diffusion system in the SIS case

## Kolmogorov-Fisher type equation

dynamics for local expectation values

$$\frac{d}{dt} \langle I_i \rangle = \beta Q \langle I_i \rangle \left( 1 - \langle I_i \rangle \right) - \alpha \langle I_i \rangle + \beta (1 - \langle I_i \rangle) \cdot \Delta \langle I_i \rangle$$

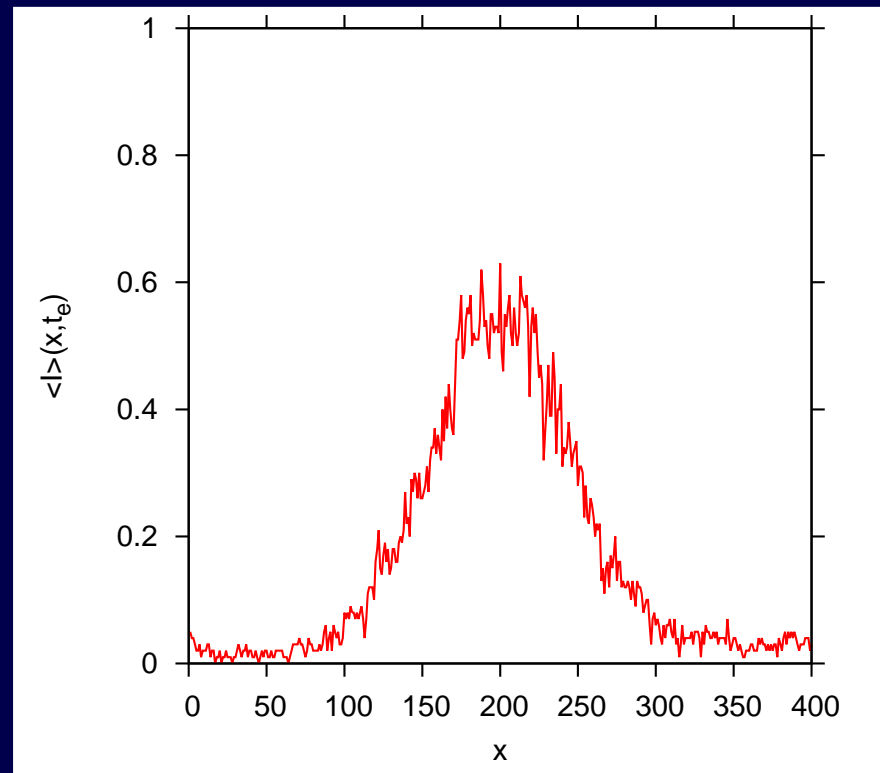


# Reaction-super-diffusion system in the SIS case

## Kolmogorov-Fisher type equation

dynamics for local expectation values

$$\frac{d}{dt} \langle I_i \rangle = \beta Q \langle I_i \rangle \left( 1 - \langle I_i \rangle \right) - \alpha \langle I_i \rangle + \beta (1 - \langle I_i \rangle) \cdot \Delta^{\frac{\mu}{2}} \langle I_i \rangle$$



# Power law jumps and power law waiting times

random walk

$$\mathbf{x}_n = \sum_{i=1}^n \xi_i \quad , \quad t_n = \sum_{i=1}^n \tau_i$$

arrival probability  $\eta(x, t)$  to have arrived at time  $t$  at the location  $x$ , jump prob.  $\lambda$ , waiting time prob.  $\psi$ ,

$$\eta(x, t) = \int_{-\infty}^{\infty} \lambda(x-x') \int_0^t \psi(t-t') \eta(x', t') dt' dx' + \delta(x) \delta(t)$$

then the probability  $p(x, t)$  to be at time  $t$  at location  $x$  via survival probability  $\Psi(t-t') := 1 - \int_{t'}^t \psi(t'') dt''$

$$p(x, t) = \int_0^t \Psi(t-t') \eta(x, t') dt'$$

with convolutions in Fourier transform respectively in Laplace transform gives

$$\tilde{p}(k, s) = \frac{1 - \bar{\psi}(s)}{s} \cdot \frac{1}{1 - \bar{\psi}(s) \cdot \tilde{\lambda}(k)}$$

# Power law jumps and power law waiting times

Fourier-Laplace transform

$$\tilde{p}(k, s) = \frac{1 - \bar{\psi}(s)}{s} \cdot \frac{1}{1 - \bar{\psi}(s) \cdot \tilde{\lambda}(k)}$$

with power law jump and waiting time probabilities for large arguments, hence for the respective transforms

$$\bar{\psi}(s) = 1 - s^\nu \quad \text{for } s \rightarrow 0$$

$$\tilde{\lambda}(k) = 1 - |k|^\mu \quad \text{for } |k| \rightarrow 0$$

with exponents  $\mu$  and  $\nu$  gives

$$\tilde{p}(k, s) = \frac{s^{\nu-1}}{s^\nu + |k|^\mu}$$

the same result as in fractional calculus

# Space-time fractional diffusion equation

generalized from  $\nu = 1$  and  $\mu = 2$

$$\frac{\partial^\nu}{\partial t^\nu} u(x, t) = \chi \frac{\partial^\mu}{\partial x^\mu} u(x, t)$$

with spatial Riesz fractional derivative via Fourier transform

$$\frac{\partial^\mu}{\partial x^\mu} e^{ikx} := -|k|^\mu \cdot e^{ikx}$$

and temporal Caputo fractional derivative via Laplace transform

$$\left( \int_0^\infty e^{-st} \left( \frac{\partial^\nu}{\partial t^\nu} f(t) \right) dt \right) := s^\nu \bar{f}(s) - s^{\nu-1} f(0)$$

we obtain as Fourier-Laplace transform

$$\tilde{u}(k, s) = \tilde{u}(k, t_0 = 0) \frac{s^{\nu-1}}{s^\nu + \chi |k|^\mu}$$

# Space-time fractional diffusion equation

solution via Laplace-back transform to Mittag-Leffler function

$$E_\nu(z) = \sum_{n=0}^{\infty} \frac{z^n}{\Gamma(\nu n + 1)}$$

with

$$\int_0^{\infty} e^{-st} E_\nu(ct^\nu) dt = \frac{s^{\nu-1}}{s^\nu - c}$$

and Fourier back-transform gives

$$u(x, t) = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{\infty} \tilde{u}(k, t_0) E_\nu(-\chi|k|^\mu(t - t_0)^\nu) e^{ikx} dk$$

# Space-time fractional diffusion equation

solution

$$u(x, t) = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{\infty} \tilde{u}(k, t_0) E_{\nu}(-\chi|k|^{\mu}(t-t_0)^{\nu}) e^{ikx} dk$$

with initial condition in real space

$$u(x, t) = \int_{-\infty}^{\infty} u(y, t_0) G(x-y, t-t_0) dy$$

with Green's function

$$G(x-y, t-t_0) = \frac{1}{\chi^{\frac{1}{\mu}}(t-t_0)^{\frac{\nu}{\mu}}} \frac{1}{2\pi} \int_{-\infty}^{\infty} e^{i\tilde{k}z} E_{\nu}(-|\tilde{k}|^{\mu}) d\tilde{k}$$

substituting  $z := \frac{x-y}{\chi^{\frac{1}{\mu}}(t-t_0)^{\frac{\nu}{\mu}}}$  and  $\tilde{k} := k\chi^{\frac{1}{\mu}}(t-t_0)^{\frac{\nu}{\mu}}$

## Fast power law random numbers

waiting times with Mittag-Leffler random numbers with exponent  $\nu$

$$\tau = -\gamma_t \ln(u) \left( \frac{\sin(\nu\pi)}{\tan(\nu\pi v)} - \cos(\nu\pi) \right)^{\frac{1}{\nu}}$$

and jumps with Lévy stable random numbers with exponent  $\mu$

$$\xi = \gamma_x \left( \frac{-\ln(u) \cdot \cos(\phi)}{\cos((1-\mu)\phi)} \right)^{1-\frac{1}{\mu}} \frac{\sin(\nu\phi)}{\cos(\phi)}$$

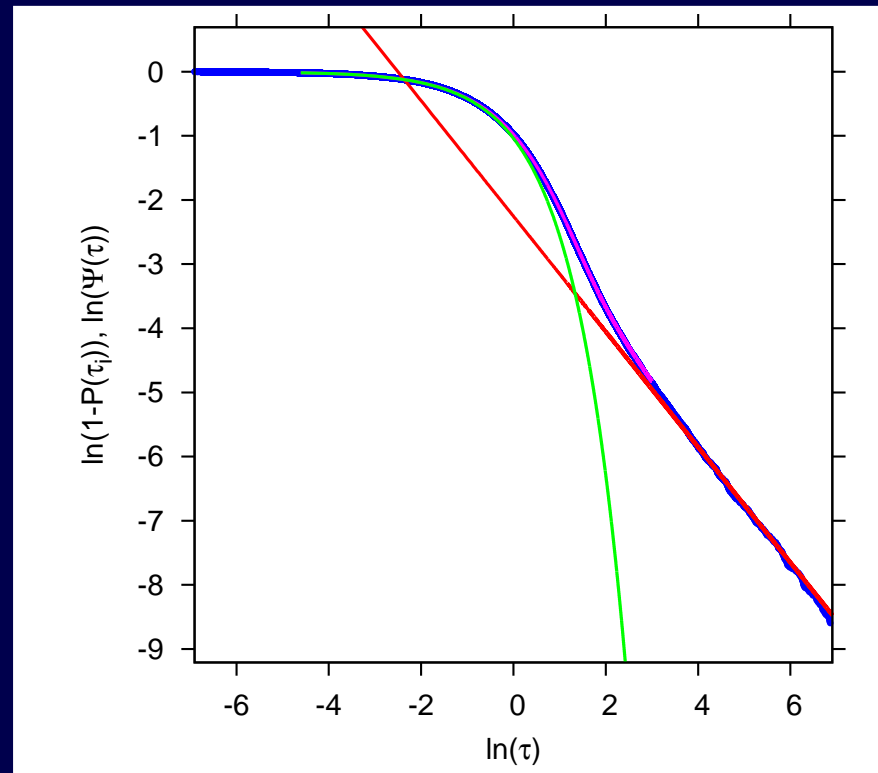
using uniformly distributed random numbers  $u$  and  $v$  on the unit interval and  $\phi := \pi \left( v - \frac{1}{2} \right)$



# Fast analysis via complementary distribution fct.

e.g. survival time distribution

$$\Psi(\tau) := \int_{\tau}^{\infty} \psi(\tilde{\tau}) d\tilde{\tau} = 1 - \int_0^{\tau} \psi(\tilde{\tau}) d\tilde{\tau} = 1 - P(\tau)$$



# Human mobility in epidemiological context

”radiation model”

uses human densities to model mobility

=> power laws expected

twitter data in Thailand

a more direct surrogate for human mobility

=> power laws observable (?)

(as import into dengue models)

# Human mobility in epidemiological models, radiation model

epidemiological models for Thai provinces  $\underline{x}_i$  and populations  $N_i$  with import  $\varrho_i$

$$\dot{\underline{X}}_i = \underline{f}_i(\underline{X}_i, \varrho_i)$$

now with explicit modelling of human mobility, hence  $T_{j|i}$  the number of people moving from location  $\underline{x}_i$  to  $\underline{x}_j$  via total number of travelers from  $\underline{x}_i$

$$T_i = \varepsilon N_i$$

assumed simplest proportional to population sizes and with elementary probability  $p_{j|i}$  for a single person to move

$$p(T_{j|i}|T_i, p_{j|i}) = \binom{T_i}{T_{j|i}} p_{j|i}^{T_{j|i}} (1 - p_{j|i})^{T_i - T_{j|i}}$$

and  $p_{j|i}$  still to be determined from detailed radiation model

## Radiation model for $p_{j|i}$

define variable  $z$  as measuring "attractivity" of a location (or "absorption capacity" in physical radiation)

draw  $N_i$  times from probability distribution  $p(z)$  obtaining maximal value  $z_i^{max}$

and use extreme value statistics tools via cumulative distribution function

$$P(z) := \int_0^z p(\tilde{z}) d\tilde{z}$$

hence for a fixed value  $z$  we have for  $N_i$  independent draws

$$\begin{aligned} p(z_i^{max} < z) &= p(z_{i,1} < z, z_{i,2} < z, \dots, z_{i,N_i} < z) \\ &= p(z_{i,1} < z) \cdot p(z_{i,2} < z) \cdot \dots \cdot p(z_{i,N_i} < z) \\ &= (P(z))^{N_i} \end{aligned}$$

## Radiation model for $p_{j|i}$

define variable  $z$  as measuring "attractivity" of a location (or "absorption capacity" in physical radiation)

draw  $N_i$  times from probability distribution  $p(z)$  obtaining maximal value  $z_i^{max}$

and use extreme value statistics tools via cumulative distribution function

$$P(z) := \int_0^z p(\tilde{z}) d\tilde{z}$$

hence for a fixed value  $z$  we have for  $N_i$  independent draws

$$p(z_i^{max} = z) = N_i \cdot P(z)^{N_i-1} \cdot p(z)$$

with  $p(z) = \frac{dP(z)}{dz}$ , hence all expressed via cumulative distribution function  $P(z)$

## Description of "absorption" process

1) Emit at  $\underline{x}_i$  a particle with attractivity value  $z_i^{max}$ .  
(The higher the population size  $N_i$  the higher  $z_i^{max}$  is likely to be).

2) Absorb not at any location  $\underline{x}_k$  with attractivity  $z_k^{max} < z_i^{max}$  in a circle with radius of distance  
 $r_{ik} := \|\underline{x}_k - \underline{x}_i\|$ .

3) Only absorb at location  $\underline{x}_j$  where the attractivity is  $z_j^{max} > z_i^{max}$  at the minimal distance  
 $r_{ij} := \|\underline{x}_j - \underline{x}_i\|$ .

## Description of "absorption" process

1) The probability  $p(z_i^{max} = z)$  of drawing  $z_i^{max}$  to be of value  $z$  at location  $\underline{x}_i$  with population size  $N_i$  is given by

$$p(z_i^{max} = z) = N_i \cdot P(z)^{N_i-1} \cdot \frac{dP(z)}{dz}$$

2) The probability  $p(\bigwedge_{k:r_{ik}<r_{ij}} z_k^{max} < z)$  of not being absorbed at any location  $\underline{x}_k$  due to  $z_k^{max} < z_i^{max}$  is given by

$$p\left(\bigwedge_{k:r_{ik}<r_{ij}} z_k^{max} < z\right) = P(z)^{s_{ij}} \quad \text{with} \quad s_{ij} = \sum_{k:r_{ik}<r_{ij}} N_k$$

3) The probability  $p(z_j^{max} > z)$  of being absorbed at nearest location  $\underline{x}_j$  with  $z_j^{max} > z_i^{max}$  is given by

$$p(z_j^{max} > z) = 1 - p(z_j^{max} < z) = 1 - P(z)^{N_j}$$

## Description of "absorption" process

hence the elementary probability  $p_{j|i}$  of being emitted in  $\underline{x}_i$  and absorbed in  $\underline{x}_j$  is given by the three contributions

$$p_{j|i} = \int_0^{\infty} p(z_i^{max} = z) \cdot p\left(\bigwedge_k z_k^{max} < z\right) \cdot p(z_j^{max} > z) dz$$



## Description of "absorption" process

hence the elementary probability  $p_{j|i}$  of being emitted in  $\underline{x}_i$  and absorbed in  $\underline{x}_j$  is given by the three contributions

$$\begin{aligned}
 p_{j|i} &= \int_0^\infty p(z_i^{\max} = z) \cdot p\left(\bigwedge_k z_k^{\max} < z\right) \cdot p(z_j^{\max} > z) dz \\
 &= \int_0^\infty N_i P(z)^{N_i-1} p(z) \cdot P(z)^{s_{ij}} \cdot (1 - P(z)^{N_j}) dz \\
 &= N_i \int_0^\infty \left( P(z)^{N_i+s_{ij}-1} - P(z)^{N_i+s_{ij}+N_j-1} \right) \frac{dP}{dz} dz \\
 &= N_i \int_0^1 \left( P^{N_i+s_{ij}-1} - P^{N_i+s_{ij}+N_j-1} \right) dP \\
 &= N_i \left( \frac{1}{N_i + s_{ij}} - \frac{1}{N_i + s_{ij} + N_j} \right) \\
 &= \frac{N_i N_j}{(N_i + s_{ij})(N_i + N_j + s_{ij})}
 \end{aligned}$$

## Mean connectivity $\langle T_{j|i} \rangle$

the mean connectivities between provinces  $\langle T_{j|i} \rangle$  are now easily obtained from the binomial probabilities

$$p(T_{j|i}|T_i, p_{j|i}) = \binom{T_i}{T_{j|i}} p_{j|i}^{T_{j|i}} (1 - p_{j|i})^{T_i - T_{j|i}}$$

with elementary probabilities  $p_{j|i}$  as calculated above

$$p_{j|i} = \frac{N_i N_j}{(N_i + s_{ij})(N_i + N_j + s_{ij})}$$

giving with  $T_i = \varepsilon N_i$

$$\langle T_{j|i} \rangle = T_i \cdot p_{j|i} = \varepsilon N_i \cdot \frac{N_i N_j}{(N_i + s_{ij})(N_i + N_j + s_{ij})}$$

to be calculated for all  $n = 76$  provinces in Thailand and its population sizes  $N_i$  and its distances  $r_{ij} := \|\underline{x}_j - \underline{x}_i\|$  from the coordinates  $\underline{x}_i$  given in the World Geodetic System 1984 (WGS 84)

# Plugging $\langle T_{j|i} \rangle$ into epidemiological models

single province models with import  $\varrho_i$

$$\underline{\dot{X}}_i = \underline{f}_i(\underline{X}_i, \varrho_i)$$

become depending on infection levels and connectivities in other provinces

$$\underline{\dot{X}}_i = \underline{f}_i(\underline{X}_i, \varrho_i(\{\langle T_{j|i} \rangle, \underline{X}_j\}))$$

e.g. in SIS model with  $S_i = (N_i - I_i)$

$$\dot{I}_i = \frac{\beta_i}{N_i}(I_i + \varrho_i N_i)S_i - \alpha_i I_i$$

becomes

$$\begin{aligned} \dot{I}_i = & \frac{\beta_i}{N_i} I_i S_i - \alpha_i I_i \\ & + \sum_{j=1, j \neq i}^n \frac{\beta_j}{N_j} I_j \cdot T_{j|i} \frac{S_i}{N_i} + \sum_{j=1, j \neq i}^n \frac{\beta_i}{N_i} T_{i|j} \frac{I_j}{N_j} \cdot S_i \end{aligned}$$

# Plugging $\langle T_{j|i} \rangle$ into epidemiological models

single province models with import  $\varrho_i$

$$\underline{\dot{X}}_i = \underline{f}_i(\underline{X}_i, \varrho_i)$$

become depending on infection levels and connectivities in other provinces

$$\underline{\dot{X}}_i = \underline{f}_i(\underline{X}_i, \varrho_i(\{\langle T_{j|i} \rangle, \underline{X}_j\}))$$

e.g. in SIS model with  $S_i = (N_i - I_i)$

$$\dot{I}_i = \frac{\beta_i}{N_i}(I_i + \varrho_i N_i)S_i - \alpha_i I_i$$

gives effective import

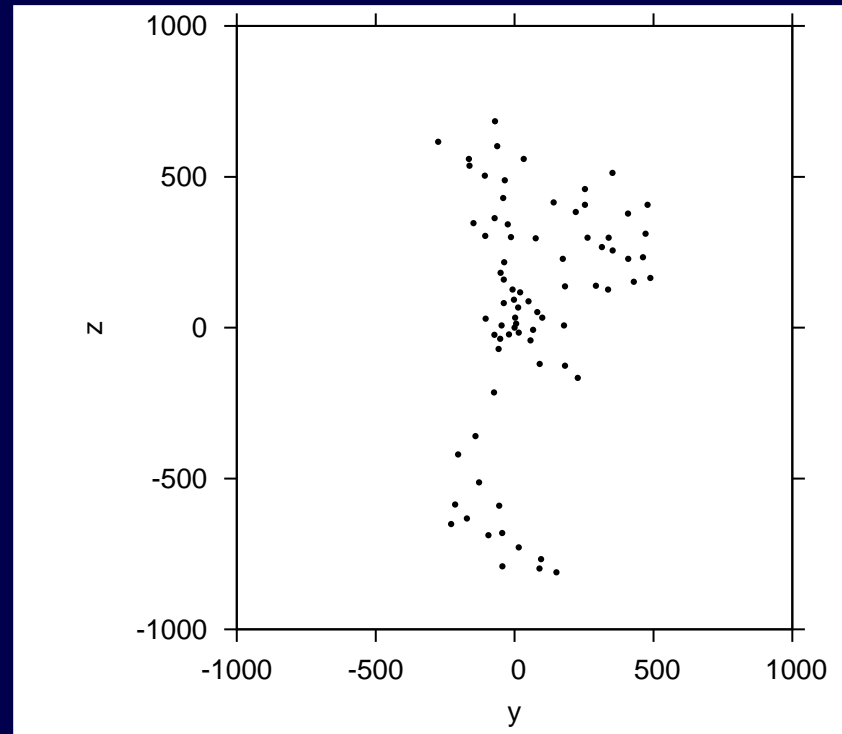
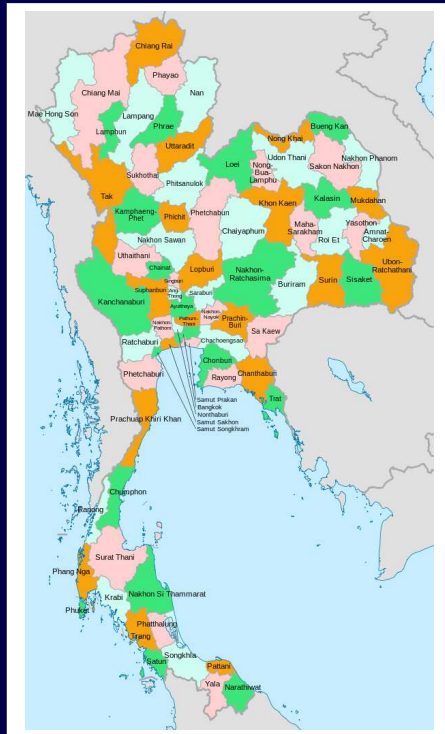
$$\varrho_i = \frac{1}{N_i} \sum_{j=1, j \neq i}^n \left( \frac{\beta_j}{\beta_i} T_{j|i} + T_{i|j} \right) \frac{I_j}{N_j}$$

# New data via DENFREE: 34 years of DHF up to today, all provinces



Thailand with 77 changwats (provinces)

# Implementation of the model for Thailand



locations  $\underline{x}_i$  and connectivities  $T_{j|i}$  calculated  
power law statistics in preparation

## One word of caution

the elementary probabilities are  $p_{j|i}$  are in the binomial distribution normalized via  $q_{j|i} := 1 - p_{j|i}$  being the probability of being emitted in  $i$  but not absorbed in  $j$ , and trivially  $p_{j|i} + q_{j|i} = 1$

but along a finite network of  $n$  nodes the  $p_{j|i}$  give

$$\sum_{j=1, j \neq i}^n p_{j|i} = \sum_{j=1, j \neq i}^n \frac{N_i N_j}{(N_i + s_{ij})(N_i + N_j + s_{ij})} = 1 - \frac{N_i}{N}$$

which is only approximately normalized in large networks with small nodes each via

$$N_i/N \rightarrow 0 \quad \text{for} \quad N_i \ll N$$

but a small probability  $N_i/N$  remains for particles to be emitted from  $i$  and not being absorbed in any other node, hence leaving any finite network